

# In the United States Court of Federal Claims

## OFFICE OF SPECIAL MASTERS

Filed: August 31, 2022

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SHANELLE MATTUS-LANG,  
*as parent and legal representative  
of her minor son, D.J.W.,*

Petitioner,

v.

SECRETARY OF HEALTH  
AND HUMAN SERVICES,

Respondent.

\* \* \* \* \*

No. 15-113V  
Special Master Sanders

Entitlement Decision; DTaP-IPV  
Vaccine; Seizure Disorder; Cognitive  
Delay; Developmental Delay; Epileptic  
Encephalopathy; Autism Spectrum  
Disorder (“ASD”); Doose Syndrome  
 (“MAE”)

*Elizabeth Martin Muldowney*, Sands Anderson, P.C., Richmond, VA, for Petitioner.  
*Camille M. Collett*, United States Department of Justice, Washington, DC, for Respondent.

### **DECISION ON ENTITLEMENT**<sup>1</sup>

On February 4, 2015, Shanelle Mattus-Lang (“Petitioner”) filed a petition pursuant to the National Vaccine Injury Compensation Program (“the Program”),<sup>2</sup> alleging that a diphtheria tetanus toxoids and acellular pertussis adsorbed and inactivated poliovirus vaccine (“DTaP-IPV”) administered on February 6, 2012, caused her minor child, D.J.W., to suffer from “a seizure disorder with cognitive and developmental delays.” Pet. at 6, ECF No. 1. Respondent filed his Rule 4(c) report on July 22, 2015, and argued that Petitioner was not entitled to compensation without “an expert report” or “other reliable medical evidence supporting causation sufficient to meet her burden of proof.” Resp’t’s Report at 10, ECF No. 18. The case proceeded to an entitlement hearing that was held on October 4–5, 2018. Min. Entry, docketed Oct. 9, 2018. At the

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<sup>1</sup> This Decision shall be posted on the United States Court of Federal Claims’ website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Decision. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

<sup>2</sup> National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all “§” references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

time of the hearing, both Petitioner and Respondent agreed that the relevant claimed injury was epileptic encephalopathy.<sup>3</sup> They also agreed that D.J.W. suffered from Doose syndrome.<sup>4</sup>

During the course of the hearing, it was revealed that an Autism Spectrum Disorder<sup>5</sup> (“ASD”) evaluation was pending. The hearing continued based upon the epileptic encephalopathy/Doose syndrome diagnosis, but the parties agreed that any subsequent autism diagnosis may necessitate additional argument and/or evidence before an entitlement decision could be rendered. In May of 2019, D.J.W. was diagnosed with autism. Pet’r’s Ex. 87 at 8, ECF No. 97. On February 7, 2020, Petitioner filed a “[b]rief in support of her contention that she be permitted to proceed in the [Program] on the claimed injury of epileptic encephalopathy despite [D.J.W.’s] subsequent autism diagnosis.” Pet’r’s Mem. at 1, ECF No. 103. On April 20, 2020, Respondent filed his response to Petitioner’s brief, including a motion for a decision dismissing Petitioner’s claim. Resp’t’s Resp. at 1, ECF No. 110. Petitioner submitted a reply to Respondent’s response on August 28, 2020. Pet’r’s Reply, ECF No. 112. On October 22, 2021, I issued an Order explaining that, after a careful review of the evidence presented, I must afford Petitioner an additional opportunity to provide expert argument and evidence “specifically and only as it relates to D.J.W.’s ASD diagnosis.” ECF No. 113. The parties then filed an additional round of expert reports and supporting medical literature. *See* Pet’r’s Exs. 88–136, ECF Nos. 114–15, 130, 133–35; Resp’t’s Exs. D, D1–D29, E, E1–E15, ECF Nos. 119–22, 124–25.

There are two predicate issues in this case: (1) can the autism diagnosis be separated from the epileptic encephalopathy diagnosis with respect to symptom onset and clinical presentation; and (2) is there preponderant evidence that the seizures (and cognitive delay) suffered by D.J.W. have an autoimmune etiology and therefore could be vaccine-caused? The success of Petitioner’s claim hinges on an affirmative answer to both questions.

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<sup>3</sup> Epileptic encephalopathy “refers to a group of disorders in which the unremitting epileptic activity contributes to progressive cerebral dysfunction.” Puneet Jain, et al., *Diagnosis and Management of Epileptic Encephalopathies in Children*, EPILEPSY RES. TREAT. (July 22, 2013), <http://dx.doi.org/10.1155/2013/501981>. The group of disorders includes Doose Syndrome/myoclonic encephalopathy. *See id.* Epileptic is defined as “pertaining to or affected by epilepsy[.]” *Dorland’s Illustrated Medical Dictionary* 1263, 633 (32nd ed. 2012) [hereinafter “*Dorland’s*”]. Epilepsy is “any of a group of syndromes characterized by paroxysmal transient disturbances of the brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system.” *Dorland’s* at 633. Encephalopathy is “atrophy of the brain.” *Id.* at 612.

<sup>4</sup> Doose syndrome is also known as myoclonic astatic epilepsy (“MAE”). MAE or Doose syndrome “is an epilepsy syndrome of early childhood, most commonly appearing between ages [one] and [five] and featuring generalized seizures. Children will experience drop attacks and staring seizures, sometimes associated with falls. MAE is idiopathic[.]” *Epilepsy Syndromes in Children*, JOHNS HOPKINS MED., <https://www.hopkinsmedicine.org/health/conditions-and-diseases/epilepsy/epilepsy-syndromes-in-children> (last visited Aug. 1, 2022). I use “Doose syndrome” and “MAE” interchangeably throughout this Decision.

<sup>5</sup> Autism Spectrum Disorder (“ASD”) as defined by the Diagnostic and Statistical Manual of Mental Disorders – 5th Edition includes “qualitative difficulties with social communication and interaction and restricted/repetitive behavior.” American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental Disorders: Fifth Edition (DSM-5)*. Arlington, VA.

After reviewing the entire record and considering both parties' arguments, I find that D.J.W.'s autism diagnosis cannot be separated from any encephalopathy diagnosis. All of the evidence that Petitioner presented prior to the revelation of D.J.W.'s autism diagnosis was in support of her argument that his developmental delays are the result of his vaccines. This was the case even though Petitioner expressed a concern about autism around the same time as the alleged vaccine-caused injuries. She continued to link all of D.J.W.'s symptoms together and argue everything was vaccine-caused, even as his ASD evaluation was pending. Now that D.J.W. has been diagnosed with autism, Petitioner continues to allege developmental delay as a vaccine-caused injury. Petitioner cites other cases wherein a child experiencing seizures was also diagnosed with autism, but for reasons explained below, those cases are not analogous to her claim. Those cases are factually distinct with respect to the onset of symptoms and the alleged vaccine-caused injuries. Furthermore, additional evidence cannot negate the fact that Petitioner's own expert has already provided the most definitive and unequivocal evidence against any argument for comorbidity in this case.

I further find that notwithstanding the comorbidity issue, there is insufficient evidence that D.J.W.'s seizures have an autoimmune etiology. D.J.W.'s relevant medical records have already been filed, and the medical literature submitted provides sufficient context for the experts' conclusions regarding the etiology and pathophysiology of D.J.W.'s condition. Petitioner asserted that D.J.W. suffers from an autoimmune epileptic encephalopathy. It follows that without an autoimmune response post vaccination, Petitioner's proposed biological mechanism is inapplicable. Petitioner's expert did not present preponderant evidence of an autoimmune encephalopathy in this case. Furthermore, Respondent's expert Dr. Holmes' assertion that Doose syndrome is widely considered to have a genetic cause, is supported by writings authored by the condition's namesake. The testimony provided by Dr. Holmes was persuasive. Also, the parties' arguments were crystalized in post-hearing briefings. Petitioner has failed to articulate a need for further evidence or argument regarding D.J.W.'s condition in the form of expert testimony or otherwise. Petitioner's claim that D.J.W.'s injuries were vaccine-caused is therefore ripe for consideration. In finding that the record is sufficiently developed, I further find that Respondent's motion to dismiss is moot. Rather than setting out the favorable inferences to Petitioner to determine if the claim is viable pursuant to the motion to dismiss standard, I will instead apply the preponderant standard under *Althen*, as articulated in Respondent's motion to dismiss, to conclude that Petitioner cannot prevail on the fully established record. Accordingly, Petitioner's claim is hereby **DISMISSED**.

## **I. Procedural History**

Petitioner filed her petition for compensation on behalf of her minor child, D.J.W., on February 4, 2015. Pet. at 1. On February 9, 2015, Petitioner submitted a notice of intent to file exhibits on a compact disc. *See* Notice, ECF No. 5. Those exhibits included two affidavits, one from Petitioner and the other from Petitioner's mother, and several medical records. Pet'r's Exs. 1–13. Petitioner filed additional medical records on April 17, 2015. Pet'r's Exs. 12–15, ECF No. 9. On May 20, 2015, Petitioner submitted additional medical records and a statement of completion. Pet'r's Exs. 16–20, ECF Nos. 14–15.

Respondent filed his Rule 4(c) report on July 22, 2015, recommending that compensation be denied. Resp't's Report at 10. Petitioner filed additional medical records on September 9, 2015. Pet'r's Exs. 21–22, ECF No. 21. On December 29, 2015, Petitioner submitted a second notice of intent to file exhibits on a compact disc. *See* Notice, ECF No. 28; Pet'r's Exs. 23–57. Those exhibits included Petitioner's expert report and curriculum vitae of Yuval Shafir, M.D., along with supporting medical literature. Pet'r's Exs. 23–57. On June 1, 2016, Respondent filed his responsive expert report from Gregory Holmes, M.D. Resp't's Ex. A, ECF No. 32.<sup>6</sup>

On October 20, 2016, Petitioner submitted an additional notice of intent to file exhibits on a compact disc. *See* Notice, ECF No. 34. These exhibits included Petitioner's supplemental expert report from Dr. Shafir and supporting medical literature. Pet'r's Exs. 58–69. Respondent filed his rebuttal expert report from Dr. Holmes on January 30, 2017. Resp't's Ex. C, ECF No. 36. This case was reassigned to me on June 20, 2017. ECF Nos. 40–41.

On August 17, 2017, I scheduled this matter for an entitlement hearing to take place from October 4–5, 2018. Order, ECF No. 45. Petitioner filed her pre-hearing brief on June 27, 2018. Pet'r's Br., ECF No. 48. Respondent submitted his pre-hearing response brief on July 27, 2018. Resp't's Resp., ECF No. 49. The entitlement hearing was held as scheduled on October 4–5, 2018. *See* Min. Entry, docketed Oct. 9, 2018.

Following the entitlement hearing, Petitioner submitted additional medical records throughout 2019, including those pertaining to D.J.W.'s autism diagnosis. *See, e.g.*, Pet'r's Ex. 87, ECF No. 97; Pet'r's Exs. 78–82, 86, ECF Nos. 79, 84, 95. Petitioner filed her post-hearing memorandum on February 7, 2020. Pet'r's Mem. at 1. On April 24, 2020, Respondent filed his response to Petitioner's memorandum, including a motion for a decision dismissing Petitioner's claim. Resp't's Resp. at 1. Petitioner submitted a reply to Respondent's response and motion on August 28, 2020. Pet'r's Reply.

On October 22, 2021, prior to ruling on Respondent's motion to dismiss, I afforded Petitioner a final opportunity to provide additional evidence regarding D.J.W.'s autism diagnosis. ECF No. 113 at 1. Petitioner filed an expert report from Dr. Shafir and supporting medical literature on this limited issue on December 1, 2021. Pet'r's Exs. 88–107, ECF Nos. 114–15. Respondent filed a responsive expert report from Dr. Holmes and medical literature on March 1, 2022. Resp't's Exs. D, D1–D29, ECF Nos. 119–21. The same day, Respondent also filed an expert report from Max Wiznitzer, M.D. Resp't's Ex. E, ECF No. 122.

On March 7, 2022, Petitioner filed a motion to strike the expert report of Dr. Wiznitzer. ECF No. 123. Petitioner argued that Dr. Wiznitzer was not previously disclosed as an expert in this case, and he did not testify at the hearing on entitlement held in October of 2018. *Id.* at 2–3. Petitioner further argued that Dr. Wiznitzer's report “is redundant and duplicative of Dr. Holmes' opinions[.]” *Id.* at 3. She continued that Dr. Wiznitzer's report “adds nothing more to the resolution of [] this case other than to produce expert opinions without the opportunity for [P]etitioner to rebut [] or cross examine the expert about these opinions.” *Id.* Petitioner argued this report would

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<sup>6</sup> Also on June 1, 2016, Respondent filed the curriculum vitae of Dr. Holmes. Resp't's Ex. B, ECF No. 31–2. This exhibit was stricken from the record and does not appear to have been re-filed. *See* Non-PDF Order, docketed June 1, 2016.

therefore be prejudicial to her case. *Id.* Respondent filed a response to Petitioner’s motion on March 15, 2022. ECF No. 126. Respondent argued that “Petitioner has not cited, and [R]espondent is not aware, of any authority that allows [P]etitioner to pick and choose the testimony [R]espondent can offer or what evidence a special master will be allowed to consider[.]” *Id.* at 4. Respondent further argued that Dr. Wiznitzer’s opinions are “well-within his expertise, his report was timely filed, and it responds to the issues that were presented very late in the development of this case[.]” namely D.J.W.’s autism diagnosis. *Id.* He further indicated that “[s]pecifically, Dr. Wiznitzer responds to opinions introduced for the first time in Dr. Shafrir’s most recent supplemental report.” *Id.* Respondent argued it would be prejudicial for Respondent to be “prevented from providing a fulsome response . . . .” *Id.* The same day, Respondent filed the medical literature referenced in Dr. Wiznitzer’s report. Resp’t’s Exs. E1–E15, ECF Nos. 124–25. Petitioner filed a reply on March 22, 2022. ECF No. 127. Petitioner reiterated her arguments in her original motion. *See id.*

I denied Petitioner’s motion to strike Dr. Wiznitzer’s expert report on March 29, 2022. ECF No. 128. I indicated that “[i]n accordance with the applicable legal principles, I am required to broadly allow the submission of evidence and will therefore afford Respondent an opportunity to defend this case.” *Id.* at 1; *see also* 42 U.S.C. § 300aa-12(d)(2); Vaccine Rule 8(c). I also noted that “when evaluating this case, I will assess Dr. Wiznitzer’s report in terms of its probative and foundational value and assign appropriate weight.” ECF No. 128 at 1–2. On April 4, 2022, Petitioner filed an unopposed motion to file a supplemental expert report in response to Drs. Holmes’ and Wiznitzer’s reports, which I granted. ECF No. 129; Non-PDF Order, docketed Apr. 13, 2022.

Petitioner filed medical records on April 18, 2022. Pet’r’s Exs. 108–10, ECF No. 130. Petitioner filed her supplemental expert report from Dr. Shafrir and supporting medical literature on June 23, 2022. Pet’r’s Exs. 111–36, ECF Nos. 133–35.

## II. Medical History

Petitioner’s son D.J.W. was born on February 27, 2007. Pet. at 1. Petitioner indicated that her son “was developing normally” and had “received previous vaccinations without apparent sequelae.” *Id.*; *see also* Pet’r’s Ex. 3 at 6–91. During the first eighteen months of his life, D.J.W. had an unremarkable medical history but suffered from various childhood illnesses. *See* Pet’r’s Ex. 3 at 6–91. D.J.W.’s medical records noted that he was healthy at his four, six, nine, twelve, fifteen, and eighteen-month well-visits. *Id.* at 7–8, 17, 36, 59, 76, 99.

On October 24, 2007, D.J.W. presented to his pediatrician Juan Garona, M.D., with a cough, ear pain, and rhinorrhea.<sup>7</sup> *Id.* at 25. He was diagnosed with an upper respiratory infection (“URI”). *Id.* On December 11, 2007, D.J.W. returned to Dr. Garona with a two to three-day history of right ear pain. *Id.* at 44. Dr. Garona diagnosed him with otitis media<sup>8</sup> and prescribed

<sup>7</sup> Rhinorrhea is “the free discharge of a thin nasal mucus.” *Dorland’s* at 1640.

<sup>8</sup> Otitis media is “inflammation of the middle ear; subtypes are distinguished by length of time from onset (*acute* versus *chronic*) and by type of discharge (*serous* versus *suppurative*).” *Dorland’s* at 1351 (emphasis in original).

Amoxicillin.<sup>9</sup> *Id.* D.J.W. suffered from three additional URIs on June 12, 2008, February 24, 2009, and May 13, 2009. *Id.* at 81–83, 117, 136–37.

On March 11, 2009, D.J.W. presented to his pediatrician for his two-year-old well-visit. *Id.* at 125–29. During this visit, Dr. Garona noted that D.J.W. “r[an], thr[ew] a ball, kick[ed] a ball, climb[ed] ladders, jump[ed], spoon fe[d him]self, shape[d] puzzles, ma[d]e [two to three-]word sentences, follow[ed] most directions well, identif[ie]d simple objects in a book, kn[ew] body parts, [and was] appropriately sociable.” *Id.* at 127.

D.J.W. underwent blood work on February 9, 2010. *Id.* at 146. The lab results showed low white blood cell count, hemoglobin,<sup>10</sup> and hematocrit.<sup>11</sup> *Id.* Nonetheless, Dr. Garona wrote that D.J.W. continued to have normal growth and development at his three-year well-visit two months later, on April 9, 2010. *Id.* at 149. He indicated that D.J.W. was taking iron supplements for his mild anemia and had a history of mild Reactive Attachment Disorder (“RAD”).<sup>12</sup> *Id.* at 149–50.

Likewise, Dr. Garona wrote that D.J.W. was a “healthy [four] year old [] male growing and developing normally[]” at his four-year-old well-visit on April 22, 2011. *Id.* at 156. Dr. Garona noted D.J.W.’s “[history] of borderline anemia.” *Id.* at 160. Dr. Garona indicated that D.J.W. knew his letters, that he engaged in make-believe play, that strangers could understand his speech, and that his fine motor skills were normal for a child of his age. *Id.* at 157–59. During this visit, D.J.W. received his measles, mumps, rubella (“MMR”) and varicella vaccinations. *Id.* at 160. Dr. Garona noted that D.J.W. had “[n]o history of significant adverse reaction [to vaccinations].” *Id.*

D.J.W. presented to a new pediatrician, George Johnson, M.D., on February 6, 2012. Pet’r’s Ex. 6 at 1. During this visit, D.J.W. received the DTaP-IPV vaccine in advance of him starting school. *Id.*

On February 13, 2012, seven days post vaccination, D.J.W. presented to the emergency room (“ER”) for a generalized seizure that occurred after he “[w]as playing on [a six-foot-tall bunk] bed, then fell.” Pet’r’s Ex. 7 at 3, 7. The ER attending noted it was “unclear if [the] seizure preceded [the] fall or [the] fall was followed by [the] seizure. From [his] parents’ history[, it was] more likely [a] fall with head trauma and [then a] subsequent seizure.” *Id.* at 7. Petitioner reported that D.J.W. experienced “[t]otal body shaking[]” with unresponsiveness, which “lasted

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<sup>9</sup> Amoxicillin is “a semisynthetic derivative of ampicillin effective against a broad spectrum of gram-positive and gram-negative bacteria; used especially in the treatment of infections due to susceptible strains of *Haemophilus influenzae*, *Escherichia coli*, *Proteus mirabilis*, *Neisseria gonorrhoeae*, streptococci (including *Streptococcus faecalis* and *S. pneumoniae*), and non-penicillinase-producing staphylococci.” *Dorland’s* at 65.

<sup>10</sup> Hemoglobin is “the red oxygen-carrying pigment of erythrocytes, formed by developing erythrocytes in bone marrow. It is a type of hemoprotein that contains four heme groups and globin and has the property of reversible oxygenation[.]” *Dorland’s* at 839.

<sup>11</sup> Hematocrit is “the proportion of the volume of a blood sample that is red blood cells[.]” *Dorland’s* at 832.

<sup>12</sup> Reactive Attachment Disorder (“RAD”) is “a mental disorder of infancy or early childhood, characterized by notably unusual and developmentally inappropriate social relatedness, usually associated with grossly pathologic care. It may be the *inhibited type*, with failure to initiate or respond to social interactions, or the *disinhibited type*, with indiscriminate sociability or attachment.” *Dorland’s* at 552 (emphasis in original).

approximately [two] minutes.” *Id.* at 3, 6. Petitioner also indicated that D.J.W. “woke up and was sluggish for a bit . . . [but had n]o vomiting or slurred speech.” *Id.* at 6. D.J.W.’s neurological examination was normal. *Id.* A CT-scan was performed in the ER, which was unremarkable. *Id.* at 8. The ER attending noted that D.J.W.’s “[s]ugar was fine and [he wa]s afebrile.” *Id.* D.J.W. was assessed with head trauma with a concussion and a seizure and was instructed to follow up with neurology. *Id.*

On March 11, 2012, D.J.W. returned to the ER for concerns of another seizure. *Id.* at 33. Petitioner reported D.J.W. experienced a loss of consciousness and that his “eyes flutter[ed] backwards in the head, [he] f[e]ll backwards onto his buttocks, [but he had] no head trauma.” *Id.* During this encounter, Petitioner reported that D.J.W. had suffered another seizure three days prior, on March 8, 2012, and “was found on the bathroom floor unconscious but then rapidly aroused.” *Id.* Petitioner reported that D.J.W. did not have a headache, fever, or chills. *Id.* The attending pediatric neurologist recommended an outpatient workup, including an EEG<sup>13</sup> and MRI, and did not prescribe medications. *Id.* at 34.

D.J.W. presented to another pediatrician, Laura Webb, M.D., on March 16, 2012. Pet’r’s Ex. 8 at 4. Petitioner reported that D.J.W. had four seizures in the past month and was now “having seizures every [three] days.” *Id.* at 4, 9. She also indicated that D.J.W. had been wetting the bed, which was “not normal for him.” *Id.* Dr. Webb consulted with neurologist Dr. Sankar during this appointment, who recommended starting D.J.W. on 10 mg/day of Keppra, an anti-seizure medication. *Id.* at 8.

On March 19, 2012, D.J.W. presented to the ER after a one to two-minute generalized tonic-clonic seizure (“GTC”),<sup>14</sup> which his father and brother witnessed. Pet’r’s Ex. 7 at 57. D.J.W. had been on Keppra for three days. *Id.* The attending ER physician noted that D.J.W. was not experiencing any “fever, chills, rash, cough, vomiting, diarrhea, or other complaints.” *Id.* His neurological examination and CT scan were normal. *Id.* at 58. The attending pediatric neurologist Ann Lewis, M.D., recommended increasing D.J.W.’s Keppra dose and instructed Petitioner to schedule a follow-up with her for D.J.W.’s continued treatment. *Id.* at 59.

Petitioner sent an email to D.J.W.’s pediatrician Dr. Webb on March 22, 2012. Pet’r’s Ex. 8 at 15. Petitioner reported that D.J.W. was having seizures every three to four days. *Id.* She expressed concerns about possible brain damage. *Id.* The same day, D.J.W. underwent an MRI of his brain, which was normal. Pet’r’s Ex. 7 at 80–81.

On March 30, 2012, D.J.W. presented to Dr. Lewis for a pediatric neurology evaluation. Pet’r’s Ex. 8 at 28. During this visit, Petitioner reported that D.J.W. “began having seizures in February[, and she] wonder[ed] if it is related to his immunizations he received one week before [the seizures began].” *Id.* at 29. Dr. Lewis wrote that D.J.W. “likely has an idiopathic localization related epilepsy.” *Id.* at 30. Dr. Lewis increased D.J.W.’s Keppra dose to 6 ml two times per day,

<sup>13</sup> D.J.W. underwent an EEG on March 21, 2012, which was normal. Pet’r’s Ex. 8 at 14.

<sup>14</sup> A generalized tonic-clonic seizure (“GTC”) is “the seizure of grand mal epilepsy, consisting of a loss of consciousness and generalized tonic convulsions followed by clonic convulsions.” *Dorland’s* at 1688. Grand mal epilepsy is “a symptomatic form of epilepsy often preceded by an aura; characterized by loss of consciousness with generalized tonic-clonic seizures[.]” *Id.* at 633.

added vitamin B6 to combat behavioral issues associated with D.J.W. taking anti-seizure medication, and discussed switching him to Trileptal<sup>15</sup> if the Keppra was ineffective. *Id.*

Petitioner contacted Dr. Lewis via email on April 7, 2012, reporting that D.J.W. experienced “another strong seizure.” *Id.* at 40. Dr. Lewis expressed that she did not think the Keppra was working well enough for D.J.W. and switched his medication to Trileptal. *Id.* at 39. Petitioner emailed Dr. Lewis again four days later, on April 11, 2012, reporting concerns with D.J.W.’s cognition. *Id.* at 50. Petitioner wrote her concerns about his “mental health[, as h]e seems to be much slower[.]” and cannot remember his colors in Spanish. *Id.* On April 16, 2012, Dr. Lewis noted that she did not “expect the seizures to be damaging [D.J.W.’s] brain[.]” *Id.* at 63. Petitioner communicated with Dr. Lewis via email again on April 23–24, 2012, noting concerns of D.J.W.’s “passing out” and staring spells. *Id.* at 69. Dr. Lewis instructed D.J.W. to stop using Trileptal and she prescribed valproic acid.<sup>16</sup> *Id.* at 82.

D.J.W. presented to Dr. Webb for his five-year-old well-visit on April 28, 2012. *Id.* at 88. Petitioner repeated concerns of D.J.W.’s cognitive decline and noted he was “forgetting things that he used to know.” *Id.* Petitioner reported that D.J.W. “‘passes out’ or seems like he is staring off into space . . . [but] Dr. Lewis believes some of this may be [a] side effect of the medications vs. new types of seizures.” *Id.*

On May 2, 2012, D.J.W. underwent a repeat EEG, which was abnormal. *Id.* at 103. The testing revealed that D.J.W. had experienced a generalized epileptic disturbance with frontal predominance. *Id.* Dr. Lewis was unable to distinguish whether this was “a truly generalized disturbance or a frontal disturbance with rapid bilateral spread.” *Id.* at 141. Later that month, on May 29, 2012, Petitioner emailed Dr. Lewis and noted a “serious decrease in [D.J.W.’s] intelligence.” *Id.* at 132.

D.J.W. presented to Dr. Lewis for a follow-up on June 6, 2012. *Id.* at 140. Dr. Lewis noted D.J.W.’s medication history to treat his seizures and wrote that despite the increased doses, she was “not able to eliminate his seizures.” *Id.* Petitioner reported continued concerns with D.J.W.’s cognitive issues, noting that D.J.W. was “talking slower, [wa]s less articulate[, and seem[ed] to have forgotten things that he knew before (more trouble counting and with letters).” *Id.* Dr. Lewis again noted that she was not certain whether D.J.W.’s cognitive decline was “secondary to medication side effects or symptomatic of an epileptic encephalopathy.” *Id.* at 141. She wrote that “[t]here are still several possibilities for [D.J.W.’s] subtype of epilepsy including Lennox-Gastaut [syndrome]<sup>17</sup> and Doose syndrome.” *Id.* Dr. Lewis discussed possible testing to look for an

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<sup>15</sup> Trileptal is the “trademark for preparation of oxcarbazepine.” *Dorland’s* at 1967. Oxcarbazepine is “an anticonvulsant used in the treatment of partial seizures[.]” *Id.* at 1355.

<sup>16</sup> Valproic acid is “a simple eight-carbon branched-chain fatty acid used as an anticonvulsant in the treatment of epileptic seizures, particularly absence seizures[.]” *Dorland’s* at 2020.

<sup>17</sup> Lennox-Gastaut syndrome is “an atypical form of absence epilepsy characterized by diffuse slow spike waves, often with atonic, tonic, or clonic seizures and intellectual disability; there may also be other neurologic abnormalities or multiple seizure types. Unlike typical absence epilepsy, it may persist into adulthood.” *Dorland’s* at 1837.

immune-related etiology and proposed additional treatments, such as IVIG and the ketogenic diet.<sup>18</sup> *Id.*

On July 11, 2012, after Petitioner reported the continued worsening of D.J.W.'s condition, Dr. Lewis wrote that she "suspect[ed D.J.W. suffered from] epileptic encephalopathy." *Id.* at 155. The next day, on July 12, 2012, Dr. Lewis had D.J.W. admitted for a repeat EEG and bloodwork to include antibody testing and a genetic epilepsy panel. *Id.* at 170. Dr. Lewis also started D.J.W. on IVIG. *Id.* D.J.W.'s admission notes indicated that Petitioner "associate[d] the onset of [D.J.W.'s] seizures to [his] vaccinations given one week prior." Pet'r's Ex. 7 at 95. D.J.W.'s repeat EEG was unchanged from his previous EEG performed on May 2, 2012, which also showed "diffuse delta slowing of the background, and a spike/wave burst during sleep." *Id.* at 99. The attending physician noted that "[t]his does not show progression (as can be seen with epileptic encephalopathies such as Lennox Gastaut)." *Id.* at 101. D.J.W.'s repeat MRI was unremarkable. *Id.* His genetic epilepsy panel also did not reveal any disease-causing mutations. Pet'r's Ex. 9 at 13. D.J.W. responded well to IVIG and was discharged on July 14, 2012, in a stable condition with medications including Keppra, Lamictal,<sup>19</sup> and valproic acid. Pet'r's Ex. 7 at 137. Dr. Lewis added Clobazam<sup>20</sup> to D.J.W.'s prescribed medications on August 16, 2012. Pet'r's Ex. 8 at 182–83.

On January 4, 2013, Petitioner contacted Dr. Webb via email and explained that D.J.W. was "not getting any better[]" and was having seventy-five drop seizures a day. *Id.* at 275. She also reported that D.J.W. experienced "a big seizure once every two weeks . . . last[ing] over [six] minutes." *Id.*

D.J.W. presented to another pediatric neurologist, Sharon McDaniel, M.D., on January 29, 2013, following the worsening of D.J.W.'s condition. Pet'r's Ex. 18 at 1. Dr. McDaniel noted that it was "difficult to classify [D.J.W.'s] epilepsy syndrome . . . [as h]e has some features compatible with myoclonic-astatic epilepsy (Doose syndrome), although he has some atypical features [] including focal/multifocal epileptiform activity in addition to generalized discharges[.]" *Id.* at 8. Dr. McDaniel adjusted D.J.W.'s medications and advised him to start the ketogenic diet. *Id.*

Petitioner spoke with Dr. Lewis regarding D.J.W.'s condition on November 1, 2013. Pet'r's Ex. 8 at 377. Petitioner reported that D.J.W. "has had a gradual increase in the frequency of his big seizures[.]" in that they occurred every couple of weeks, increased to every week, and then to every two to three days. *Id.* Dr. Lewis noted that Petitioner had not been checking D.J.W.'s urine ketones to monitor his consistency with the ketogenic diet, so Dr. Lewis "c[ould not] use that as a measure of change in [D.J.W.'s] compliance." *Id.* Petitioner acknowledged that D.J.W. may have cheated on this diet around Halloween. *Id.* Dr. Lewis wrote that if that was the case, D.J.W. may take one to two weeks to return to baseline. *Id.*

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<sup>18</sup> The ketogenic diet is "a diet that contains a large amount of fat with minimal amounts of protein and carbohydrate, in order to produce ketosis[.]" *Dorland's* at 516.

<sup>19</sup> Lamictal is the "trademark for a preparation of lamotrigine." *Dorland's* at 1000. Lamotrigine is "an anticonvulsant used in the treatment of partial seizures in adult patients formerly treated with an enzyme-inducing anticonvulsant (e.g., carbamazepine) and as an adjunct in the treatment of partial seizures in adults with epilepsy and of generalized seizures associated with Lennox-Gastaut syndrome[.]" *Id.* at 1003.

<sup>20</sup> Clobazam is "a benzodiazepine with anticonvulsant actions; administered orally as an adjunct in the treatment of epilepsy." *Dorland's* at 373.

The next day, on November 2, 2013, D.J.W. returned to Dr. Webb with complaints of “an increase in seizure activity resulting in multiple falls and hits to his head.” *Id.* at 385. D.J.W.’s grandmother attended this appointment with him and noted that D.J.W. had been in a constant state of staring for the past two days. *Id.* She also reported that D.J.W. could not walk or use the bathroom by himself. *Id.* Dr. Webb advised D.J.W. to go to the ER to be monitored. *Id.* at 386. During his hospitalization, D.J.W.’s mental status and neurological examination were normal. Pet’r’s Ex. 7 at 208. D.J.W. was discharged home on November 4, 2013, and Clonazepam<sup>21</sup> was added to his prescribed medications. *Id.* at 210.

D.J.W. underwent a repeat EEG on April 8, 2014. Pet’r’s Ex. 8 at 413. The results of the EEG remained unchanged and showed generalized spike and wave complexes during D.J.W.’s sleep. *Id.*

On June 25, 2014, D.J.W. returned to Dr. Lewis for a follow-up. *Id.* at 447. Dr. Lewis wrote that “[o]verall, [D.J.W.] has done well with the ketogenic diet[,]” although “[h]e has had ups and downs[.]” *Id.* at 448. She also noted that D.J.W.’s “seizures are much worse for about a week[.]” when he “cheats” on the ketogenic diet. *Id.* Dr. Lewis wrote that D.J.W. was experiencing a grand mal seizure “every week (in [his] sleep), drop seizures [zero to two times a day] on a good day and [ten to fifteen times a day] on a ‘bad day[,]’ and no absence/staring spells.” *Id.* She indicated that D.J.W.’s “cognitive function ha[d] improved with his current level of seizure control (and [being] off of valproic acid and benzos).” *Id.* at 450. Dr. Lewis noted D.J.W.’s difficulties with learning. *Id.* at 448. She concluded that “Doose syndrome seems to be the most appropriate diagnosis[.]” for D.J.W.’s condition. *Id.* at 450. Dr. Lewis advised Petitioner to continue D.J.W.’s current medications and ketogenic diet. *Id.*

D.J.W. attended follow ups with pediatrician Dr. Garona throughout 2018. *See* Pet’r’s Ex. 108 at 8–11, ECF No. 130. He also presented for neurology follow ups with various treaters for his epileptic encephalopathy. *Id.* at 11–16. No cause of D.J.W.’s condition was identified absent Petitioner’s self-reported concern that his injuries were vaccine-caused. *See id.* at 15, 20. A repeat EEG performed on September 24–25, 2018, showed abnormal results. *Id.* at 7. The impression included a “[d]iffusely slow background. Delta-range slowing is particularly prominent in the frontal regions bilaterally hi [sic] again . . . multifocal epileptiform discharges . . . generalized spike and slow-wave complexes . . . [and] bilateral, frontally predominant ‘paroxysmal fast activity[.]’” *Id.* This study “suggest[ed] a severe underlying epileptogenic disturbance and is consistent with [D.J.W.’s] diagnosis of epileptic encephalopathy.” *Id.*

On January 10, 2019, after years of continuous treatment for his Doose syndrome, D.J.W. was seen by Aaron Nayfack, M.D., a developmental behavioral pediatrician, on referral from his pediatrician. Pet’r’s Ex. 82 at 11, ECF No. 84. Dr. Nayfack recommended an Autism Spectrum Disorder evaluation “following seizure activity at 5 years [old] and related regression in functioning.” Pet’r’s Ex. 86 at 5, ECF No. 95. Dr. Nayfack noted that he “underst[oo]d the concern for autism but [he was] not sure if it is the cause of [the] observed delays.” Pet’r’s Ex. 82 at 34. He continued that D.J.W.’s “long seizure history is the main driver but [agreed] there is definitely

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<sup>21</sup> Clonazepam is “a benzodiazepine used as an anticonvulsant in the treatment of Lennox-Gastaut syndrome and of atonic and myoclonic seizures and as an anti[-]panic agent in the treatment of panic disorders[.]” *Dorland’s* at 373.

at least one secondary diagnoses [sic] to be considered. The main possibilities in [his] mind [we]re autism, intellectual disability or both.” *Id.*

D.J.W. presented to clinical psychologist Carrie Silver, Ph.D., on May 22, 2019. Pet’r’s Ex. 86 at 1. She noted under chief concerns: “[a] review of well[-]child checks from ages 2, 3[,] and 4 reveal no developmental concerns.” Pet’r’s Ex. 87 at 1, ECF No. 97. Dr. Silver considered all of D.J.W.’s symptoms in her assessment and wrote, “[s]ince seizures began at age 5, [D.J.W.] has stalled in his development and regressed in many ways.” *Id.* She also noted that despite starting a ketogenic diet, he continues to have seizures. *Id.* Dr. Silver wrote that the seizures “seem to also coincide with memory loss of information [he] previously retained.” *Id.* at 2.

D.J.W. underwent testing to assess his intellectual functioning and was determined to be within the extremely low range of ability in all five tested areas. *Id.* at 3–4. As a result, Dr. Silver concluded that “[g]iven the full picture and review of available data, it is determined that [D.J.W.] does meet [the] medical diagnostic criteria for an Autism Spectrum Disorder [diagnosis].” *Id.* at 7. Specifically, Dr. Silver wrote that he “present[s] with behavioral aspects of an Autism Spectrum Disorder including repetitive play patterns, rigidity[,] and hyposensitivity to pain. He has substantial delays in imaginative and creative play[,] . . . tends to resist interacting with other children[, and exhibits s]ome difficulty with conversation[.]” *Id.* D.J.W. was diagnosed at a Level 2 on the spectrum, indicating that he requires “substantial support.” *Id.*

On January 29, 2020, D.J.W. presented for a neurology follow-up with Jane MacLean, M.D., and she noted his “[r]ecent diagnosis of ASD.” Pet’r’s Ex. 108 at 28. D.J.W. returned on March 9, 2020, and was still “having a lot of seizure activity.” *Id.* at 33. The working diagnoses included “Lennox-Gastaut syndrome, intractable, with status epilepticus[.]” *Id.* at 4. The same day, March 9, 2020, D.J.W. had a follow-up with Dr. Nayfack. Pet’r’s Ex. 109 at 27, ECF No. 130. Dr. Nayfack maintained his impression of “moderate [intellectual disability] and autism.” *Id.* at 28. He based this assessment on D.J.W.’s “clinical impressions, parent report[s], and previous evaluations[.]” which noted “the core deficits we see in all children with autism, including difficulty interacting socially[, . . .] communicating with others[,] and restrictive/repetitive behaviors.” *Id.* at 35. He noted that D.J.W. “demonstrate[d] some improvement with a school program that includes speech, [occupational therapy,] and [adapted physical education].” *Id.* at 27. D.J.W. presented for follow-ups throughout 2020. Pet’r’s Ex. 108 at 34–51. On December 16, 2020, D.J.W. was diagnosed with asthma. *Id.* at 52. Dr. MacLean noted D.J.W.’s diagnoses of “refractory generalized epilepsy with epileptic encephalopathy[,] intellectual disability[,] and [ASD]” on November 9, 2021. *Id.* at 59. He continued to receive care for his conditions throughout 2021 and 2022. *See id.* at 52–67.

### **III. Expert Qualifications**

#### **a. Petitioner’s Expert, Dr. Yuval Shafrir, M.D.**

Dr. Shafrir received his medical degree from the Sackler School of Medicine in Tel Aviv, Israel in 1982. Pet’r’s Ex. 24 at 1. He completed his post-graduate training at the Chaim Sheba Medical Center in Tel Hashomer, Israel, where he completed a rotating internship in 1983. *Id.* Dr. Shafrir completed residencies in pediatrics at the Kaplan Hospital in Rehovot, Israel and the

Beilinson Medical Center in Petah Tikvah, Israel in 1984 and 1985, respectively. *Id.* He completed an additional pediatric residency in the United States at North Shore University Hospital in Manhasset, New York in 1988. *Id.* Dr. Shafrir also completed a pediatric neurology residency and fellowship at the Washington University Medical Center in St. Louis, Missouri in 1991. *Id.* The following year, in 1992, Dr. Shafrir completed a fellowship in pediatric neurophysiology and epileptology at the Comprehensive Epilepsy Center at Miami Children’s Hospital. *Id.* He became board certified in neurology and psychiatry with a special qualification in child neurology in 1993, followed by neurophysiology in 1998. *Id.* at 2. Following active duty as a Major in the U.S. Army’s Medical Department from 1993–1995, Dr. Shafrir was an attending child neurologist at Georgetown University Hospital and Oklahoma University Health Science Center from 1995–1999 and 1999–2000, respectively. *Id.* at 2–3. Dr. Shafrir served as an associate professor of neurology and pediatrics while at both institutions. *Id.* at 3. Since 2000, Dr. Shafrir has practiced in the field of pediatric neurology in private practice. *Id.* He currently serves as an assistant professor of pediatrics at the University of Maryland School of Medicine. *Id.* He also teaches residents at Sinai Hospital’s Department of Pediatrics. *Id.* Dr. Shafrir’s curriculum vitae includes approximately twenty published articles and abstracts of which he is a listed author. *See id.* at 4–7.

During the hearing, Dr. Shafrir stated that the “main focus” of his clinical practice involves epilepsy. Tr. 72:16. He also noted that “in the last [twenty] years[, he has seen] a lot of patients with more neurological problems . . . and then . . . autisms [sic].” Tr. 72:9–12. He stated that he has also dealt with patients who have Doose syndrome of “both the easy variety and severe variety.” Tr. 73:3–7. He also stated that he has testified many times in the Vaccine Program. Tr. 73:16–22.

Dr. Shafrir submitted two expert reports and testified during the hearing. *See* Pet’r’s Exs. 23, 58; Tr. 71:8–226:4. Dr. Shafrir was offered by Petitioner as an expert in pediatric neurology without objection, and I recognized him as such. Tr. 73:23–25, 74:1–2. Following the entitlement hearing, Dr. Shafrir submitted two supplemental expert reports. *See* Pet’r’s Exs. 88, 111.

#### **b. Respondent’s Expert, Dr. Gregory Holmes, M.D.**

Dr. Holmes received his medical degree from the University of Virginia School of Medicine (“UVA”) in 1974, along with an honorary degree from Harvard University in 1996. Resp’t’s Ex. B at 1. He completed his post-graduate training at Yale University School of Medicine, where he completed an internship in pediatrics in 1975 and a residency in pediatrics in 1976. *Id.* Dr. Holmes also completed a residency in neurology at UVA in 1979. *Id.* He is board certified in pediatrics, psychiatry, neurology with special competence in child neurology, and clinical neurophysiology. *Id.* He served as an associate professor of neurology and pediatrics at Harvard Medical School from 1988–1996, before serving as a professor of neurology at the same institution from 1996–2002. *Id.* at 2. Dr. Holmes was also a professor of neurology and pediatrics at Dartmouth Medical School from 2002–2013. *Id.* He currently serves as a professor and Chairman of Neurological Sciences at the University of Vermont College of Medicine, as well as a professor of pediatrics. *Id.* Dr. Holmes served as the Director of the Clinical Neurophysiology Laboratory and Epilepsy Program at the Children’s Hospital in Boston, Massachusetts for

approximately ten years, from 1988–1998. *Id.* Dr. Holmes’ curriculum vitae includes over six hundred articles, reviews, and abstracts of which he is a listed author. *See id.* at 39–113.

During the hearing, he explained that as the Chairman of the Department of Neurological Sciences, he “teach[es] students and train[s] physicians on seizure and seizure disorders, epilepsy, and epileptic encephalopathy[.]” Tr. 240:21–25, 241:1. He also stated that throughout his clinical practice, he has treated ten to fifteen patients with Doose syndrome. Tr. 242:8–12.

Dr. Holmes submitted two expert reports and testified during the hearing. *See* Resp’t’s Exs. A, C; Tr. 239:18–312:11. Dr. Holmes was offered by Respondent as an expert in pediatric neurology without objection, and I recognized him as such. Tr. 242:23–25, 243:1–4. Following the entitlement hearing, Dr. Holmes submitted an additional expert report. *See* Resp’t’s Ex. D.

#### **c. Respondent’s Expert, Dr. Max Wiznitzer, M.D.**

Dr. Wiznitzer obtained his medical degree from Northwestern University in 1977. Resp’t’s Ex. F at 1. He then completed a residency in pediatrics at Children’s Hospital Medical Center in Cincinnati, Ohio, followed by fellowships at the Cincinnati Center for Developmental Disorders, in pediatric neurology at the Children’s Hospital of Philadelphia, and in higher cortical functions at the Albert Einstein College of Medicine. *Id.* at 1–2. He is currently a pediatric neurologist at University Hospitals of Cleveland, as well as a professor of pediatrics and neurology at Case Western University. Resp’t’s Ex. E at 1. He is board certified in pediatrics, psychiatry, neurology (with a special qualification in child neurology), and neurodevelopmental disabilities. *Id.* He is a part of the epilepsy group at University Hospitals Case Medical Center, UH Rainbow Babies, and Children’s Hospital. *Id.* Dr. Wiznitzer has an active clinical practice interpreting EEGs and treating pediatric patients who have seizure disorders and epileptic encephalopathies. *Id.* He serves on the professional advisory board of the Autism Society of Ohio, is a child neurology liaison to the American Academy of Pediatrics’ Autism Subcommittee, and is the American Academy of Pediatrics’ neurology liaison to the Autism Treatment Network. *Id.* at 2. He is on the editorial board of several journals, including the Journal of Child Neurology, Lancet Neurology, and Pediatric Neurology. *Id.* He has authored or co-authored eleven textbook chapters and over eighty scientific papers. *Id.* Dr. Wiznitzer submitted one written expert report in this case. *See id.*

### **IV. Petitioner’s Claim and Respondent’s Response**

Petitioner alleged in the petition that D.J.W. suffered from “a seizure disorder with cognitive and developmental delays, which were caused in fact by his receipt of the DTaP-IPV vaccine.” Pet. at 6. As the case proceeded to the entitlement hearing, Petitioner further defined her claim in a pre-hearing briefing and explained that D.J.W. suffers from an “autoimmune epileptic encephalopathy that progressed into a severe epileptic syndrome with associated developmental delay[.]” following his DTaP-IPV vaccinations. Pet’r’s Br. at 9. During the entitlement hearing, Petitioner’s expert Dr. Shafrir opined that D.J.W. developed a “progressive and severe and disabling epileptic encephalopathy.” Tr. 75:24–25. Dr. Shafrir continued that D.J.W. “has the absolute typical epileptic encephalopathy in which the seizures is [sic] contributing to his cognitive and neurological decline[,] and emotional decline and emotional symptoms, and we do[ not] have any other cause other than the epilepsy itself to cause it.” Tr. 131:10–14. Dr. Shafrir concluded

that this encephalopathy “is more likely than not [to] have [an] immune basis,” and “that the vaccine was the trigger.” Tr. 76:1–2.

Post hearing, D.J.W. was diagnosed with autism. *See generally* Pet’r’s Ex. 86. In her post-hearing memorandum, Petitioner reiterated that her claim “is that D.J.W. suffered a vaccine injury, namely epileptic encephalopathy (i.e.,] Doose syndrome), via an autoimmune process.” Pet’r’s Mem. at 11. She asserted that “petitioners in the National Vaccine Injury Compensation Program have previously pursued claims based upon an encephalopathy by a covered vaccine that later manifested developmental regression or even autism.” *Id.* at 11–12 (citing *Wright v. Sec’y of Health & Hum. Servs.*, No. 12-423V, 2015 WL 6665600, at \*98 (Fed. Cl. Spec. Mstr. Sept. 21, 2015)). Petitioner argued that based on the reasoning in similar cases, “[her] claim is viable despite an ASD diagnosis[,] and [P]etitioner should be permitted to proceed on this injury.” Pet’r’s Mem. at 13.

Respondent addressed Petitioner’s memorandum with a response, including a motion to dismiss, and asserted that “there is no credible evidence that vaccinations cause autism, and there is no manner to proceed that excludes D.J.W.’s autism diagnosis from his epileptic encephalopathy.” Resp’t’s Resp. at 11. He argued D.J.W. has autism and Doose syndrome, two “conditions [that] are inherent encephalopathies of the brain and can be understood as generalized brain disorders.” *Id.* at 8. Respondent continued that “the two entities are so intertwined that it is impossible to separate them.” *Id.* at 9. Respondent noted that “Petitioner’s argument here that [D.J.W.’s] ‘neurologic’ [sic] and other developmental problems, which have been subsequently diagnosed as autism, are the product of a vaccine-aggravated epileptic encephalopathy is a tactical approach to evade well-established precedent that vaccines do not cause autism.” *Id.* He argued that Petitioner is now attempting to “recast [the] claim that a vaccine caused autism into an encephalopathy claim based on the logic that the neurologic symptoms associated with an ASD reflect an underlying brain injury.” *Id.* Respondent asserted that this is an autism injury case and given the history of such claims in the Program, “the current record fails to provide evidence [of] a reasonable basis for bringing, or moving forward with, this claim.” *Id.* at 12.

Petitioner argued in her reply to Respondent’s response that she is “not attempting to recharacterizing [sic] an autism diagnosis as an encephalopathy as argued by [R]espondent[.]” Pet’r’s Reply at 3. Petitioner emphasized that she is alleging only that D.J.W.’s encephalopathy is vaccine caused. *Id.* She stated that “[t]he court is not required to find that [D.J.W.’s] subsequent diagnosis of autism was or was not caused by the vaccination.” *Id.* Petitioner conceded that she must address D.J.W.’s autism diagnosis. *Id.* at 3–4. She asserted that “additional expert testimony [wa]s necessary and relevant to the determination as to the issue of whether [P]etitioner’s claim that D.J.W.’s vaccine induced epileptic encephalopathy is separate and distinct from [his] subsequent autism diagnosis.” *Id.* at 4. She reiterated that her claim is based on an encephalopathy diagnosis, “and there is no dispute” between the parties that D.J.W. “developed epileptic encephalopathy[] or unremitting epileptic activity that contributed to his severe and rapid cognitive and behavioral impairments, after his vaccination with DTaP-IPV on February 6, 2012.” *Id.* at 3.

## **V. D.J.W.’s Diagnoses**

### **a. Autism Spectrum Disorder**

D.J.W. was diagnosed with ASD on May 22, 2019, at twelve years old. For several years prior, Petitioner communicated to D.J.W.'s medical providers that she had "long been concerned about a possible Autism Spectrum Disorder [diagnosis] further complicating [D.J.W.'s] developmental functioning." Pet'r's Ex. 86 at 6. During D.J.W.'s ASD evaluation, Petitioner told Dr. Silver that D.J.W.'s "onset of symptoms [] corresponds to seizure activity rather than prior to the age of [five] while [he] was navigating earlier milestones." *Id.* Petitioner testified during the October 4, 2018 hearing, that she could not remember specific dates but that she asked D.J.W.'s treaters about the cause of his cognitive symptoms after she "noticed his brother was developing faster." Tr. 33:5. She stated, "doctors sa[id] that the seizures could be causing delays but then also that his delays could be caused by, you know, him having autism." Tr. 34:9–11. Since the seizures started "he[ had been] having a lot of activity while he[ is] sleeping, so even the ones that [Petitioner was] not catching, he[ was] still having them, and those are causing, you know issues . . . it[ is] very confusing, like we do[ not] – honestly do[ not] know what[ is] – what[ is] wrong with [D.J.W.]" Tr. 35:6–11.

Petitioner's expert testified after hearing Petitioner's account and unequivocally ruled out autism as a diagnosis or comorbidity. He stated, "first of all, [the child] does not have autism." Tr. 146:11. Dr. Shafrir explained that his contention is largely based on the age of autism onset, typically around or before the age of three. Tr. 146:12–13. D.J.W.'s symptoms consistent with autism manifested "[a]fter the onset of his encephalopathy. Not before. And after the onset of his seizures. Not before." Tr. 148:12–14. He explained that autism "is a neurological manifestation of multiple diseases and at least is — at least 150 conditions [] cause autism." Tr. 146:23–25. When asked if a patient can have autism concurrent with seizure disorders, Dr. Shafrir said no. Tr. 148:18–20. He stated that "seizure[s] cause autistic symptoms. That[ is] what happens. This is a part of epileptic encephalopathy." Tr. 148:20–21. Petitioner's expert was clear, "[a]utism is not an independent symptom that you have in addition to having epileptic encephalopathy independently." Tr. 149:2–4. Dr. Shafrir said that he "never heard anybody claim it anyway." Tr. 149:4–5. Dr. Shafrir reiterated his position that "[a]utism is not an additional independent diagnosis in a patient who have [sic] already known severe progressive — regressive epileptic encephalopathy." Tr. 150:13–15.

Dr. Shafrir submitted a post-hearing expert report following D.J.W.'s ASD diagnosis, wherein Dr. Shafrir maintained that autism is not applicable in this case. *See* Pet'r's Ex. 88 at 37. He wrote that "D.J.W.'s clinical presentation, including his autistic symptoms can be fully explained by the diagnosis of Doose syndrome." *Id.* at 39. Dr. Shafrir cited to the CDC reference on autism,<sup>22</sup> which states, "ASD begins before the age of [three] years." *Id.* at 38; Pet'r's Ex. 93 at 1, ECF No. 114. He highlighted that according to Dr. Silver, D.J.W.'s "development was typical" and he had "no developmental concerns" prior to seizures that began at five-years-old. Pet'r's Ex. 88 at 38; *see also* Pet'r's Ex. 86. Dr. Shafrir continued that Dr. Silver associated D.J.W.'s stalled development and regression with these seizures. *See* Pet'r's Ex. 88 at 31. He stated definitively that "[ASD] never starts at the age of [twelve]," and described D.J.W.'s late diagnosis as "a result of lack of knowledge, experience[,] and understanding of the nature of [ASD], as well as the diagnostic process by the single psychologist who made the diagnosis." *Id.* at 36, 45. Dr. Shafrir continued his criticism of Dr. Silver and stated that she "failed to cover the entire diagnostic

<sup>22</sup> *Signs and Symptoms of Autism Spectrum Disorder*, CENTERS FOR DISEASE CONTROL AND PREVENTION, <https://www.cdc.gov/ncbddd/autism/signs.html>.

list in the DSM-V,” and she “contradicted her own scoring . . . which indicated that D.J.W. scored below the cutoff for an autism spectrum disorder.” *Id.* at 46.

Respondent’s expert Dr. Holmes was not allowed to testify about the pending ASD evaluation.<sup>23</sup> Dr. Holmes did note that D.J.W. had an atypical presentation of Doose syndrome that would account for his symptoms, but he was not including in his assessment the behavioral and cognitive delays that Petitioner expressed concern about. Tr. 314:1–6. Dr. Holmes also pushed back on the implication from Dr. Shafrir that seizures can cause autistic-like symptoms. Dr. Holmes then submitted a post hearing expert report in response to Dr. Shafrir and agreed with Dr. Silver’s amended diagnosis, “autism spectrum disorder with severe intellectual impairment, moderately severe language impairment, associated with Doose.” Resp’t’s Ex. D at 2. Dr. Holmes also filed literature that discusses the “substantial evidence that genetics plays an important role in [the development of] ASD.” Resp’t’s Ex. D2 at 1, ECF No. 119.<sup>24</sup>

In response to Dr. Shafrir’s focus on the age of onset, Dr. Holmes submitted the 2018 consensus guidelines from the British Association for Psychopharmacology to note that the current DSM-5 “does not specify an age of onset.” Resp’t’s Ex. D3 at 8, ECF No. 119.<sup>25</sup> The revision also states that “symptoms must be present in the early developmental period,” but that “ASD may not become fully apparent until later in life and enables the diagnosis of ASD [even into] adulthood.” *Id.* The article continues that diagnosis should be conducted by a multi-disciplinary team of professionals “trained in the assessment, diagnosis, and treatment of ASD using a combination of diagnostic tools . . . .” *Id.* at 33. The authors identify speech and language therapists, clinical psychologists, pediatricians, psychiatrists, and occupational therapists as ideal team members. *Id.*

Post hearing, Respondent filed an expert report from pediatric neurologist Dr. Max Wiznitzer that directly addresses the late ASD diagnosis in this case. *See* Resp’t’s Ex. E. Dr. Wiznitzer conceded that most children are symptomatic by age three, but noted that “there are some, such as D.J.W., who have a developmental regression and become symptomatic after that age and during the early childhood years.” *Id.* at 9. He noted that the DSM-5 now includes within ASD: childhood disintegrative disorder, Asperger’s disorder, and pervasive developmental disorder not otherwise specified. *Id.* Because one or more of these conditions is characterized by a “clinically significant loss of previously acquired skills (before age [ten] years),” Dr. Wiznitzer opined that “D.J.W.’s onset of ASD falls within the accepted age range of onset.” *Id.*

## **b. Doose Syndrome**

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<sup>23</sup> D.J.W.’s upcoming ASD evaluation was not disclosed prior to the entitlement hearing, and instead was revealed during the hearing. That was not the injury alleged in the petition or any subsequent pleadings, and there was no testimony, written or otherwise, relating to an autism diagnosis in advance of the hearing in this case.

<sup>24</sup> A.W. Buckley & G.L. Holmes, *Epilepsy and Autism*, 6 COLD SPRING HARB PERSPECT MED. 1–18 (2016).

<sup>25</sup> O.D. Howes, et al., *Autism Spectrum Disorder: consensus guidelines on assessment, treatment and research from the British Association for Psychopharmacology*, 32(1) J. PSYCHOPHARMACOL. 3–29 (2018).

Dr. Shafrir opined during the hearing that D.J.W.'s encephalopathy was autoimmune in nature and, more specifically, Doose syndrome with a "very early loss of cognitive function." Tr. 76:8–9. Dr. Shafrir explained that D.J.W.'s Doose syndrome diagnosis is "based on [D.J.W.'s] EEG and the predominance of [his] atonic seizures[.]" Tr. 90:10–11. He then equivocated and noted that D.J.W.'s treaters "decided that it fits Doose the best, and — but, as I said, this is — this is a — less than half of the patient with Doose that — they have some — I mean, it[ is] not there." Tr. 90:10–14. Dr. Shafrir continued, "I think that his diagnosis is Doose syndrome of the severe variety with very early progression and severe neurological impairment, regression, cognitive function, which appeared very early in his course." Tr. 90:20–23. Dr. Shafrir maintained his opinion (post hearing) that D.J.W. only has Doose syndrome, despite the ASD diagnosis. *See* Pet'r's Ex. 88.

Respondent's expert Dr. Holmes agreed with D.J.W.'s diagnosis of epileptic encephalopathy, but he was equivocal when asked specifically about Doose syndrome. Dr. Holmes described the Doose syndrome in this case to be a typical case of a rare, unfavorable presentation and outcome. Tr. 253:11. Dr. Holmes described D.J.W.'s first seizure:

[D.J.W.] was a healthy, normal child, four years old, who had a single seizure. He fell when he was climbing up to the bed, hit his head, had a generalized tonic-clonic seizure which lasted approx. [sic] — a couple of minutes. It was followed by a postictal period. And then he returned to his baseline relatively quickly. And the physicians in the emergency room were concerned about the head trauma part of it and then did a CT scan, which was normal.

Tr. 256:4–11.

Dr. Holmes continued that D.J.W. "was then discharged home and did well with no evidence of any type of encephalopathic process occurring until approximately one month later[.]" when Petitioner believed D.J.W. had another seizure in the bathroom. Tr. 256:12–14. Petitioner did not take D.J.W. to the hospital following the second seizure, but "a few days later, [there was] another clear-cut generalized tonic-clonic seizure," prompting an epilepsy classification after two spontaneous seizures less than one month apart. *See* Tr. 256:17–18. Dr. Holmes opined that it "would be extremely unusual in a child that has an autoimmune cause, for their first seizure to [be] an isolated seizure." Tr. 256:25, 257:1–2. Dr. Holmes noted D.J.W.'s normal EEG and that he "demonstrated no signs of any type of encephalopathy." Tr. 256:23–24.

Although there was no family history or positive genetic testing in D.J.W.'s case, Dr. Holmes explained that "the prevalence of specifically myoclonic and astatic seizures among family members is [significantly higher than the general population, but still] found to be only [two] percent." Tr. 254:5–8. He noted that D.J.W. had "[n]ormal development before onset. Never neurometabolic or degenerative diseases. Mostly no neurological deficits at the onset of the epilepsy." Tr. 252:14–16. He continued that there were "[p]rimarily generalized myoclonic, astatic or myoclonic-astatic seizures, short absences[, and] mostly generalized tonic-clonic seizures [and] rarely focal seizures." Tr. 252:18–21. Dr. Holmes also referred to the testimony of Petitioner's mother who indicated that "if [her grandson] did[ not] have a seizure before 7:00 a.m. that he was[

not] going to have one.” Tr. 269:24–25. Dr. Holmes referenced the Nabbout and Dulac article<sup>26</sup> to support his contention that D.J.W. suffers from a severe case of Doose syndrome. Resp’t’s Ex. A, Tab 3, ECF No. 50. The authors wrote:

[MAE/Doose syndrome] affects previously normal children, mainly boys, with a high incidence of familial incidence of familial antecedents of epilepsy. It begins between 2 and 5 years of age, with some patients having a few earlier febrile convulsions. Generalized tonic-clonic seizures are the only type of seizures during the first few months of the disease. Then, myoclonic astatic seizures occur with increasing frequency, causing the patient to fall several times a day. . . . Between 2 and 12 months after onset, the other half of the patients [with more severe manifestation and less favorable outcome] have an epileptic encephalopathy with mental deterioration, erratic myoclonus, and vibratory tonic seizures, especially on early morning sleep, confusion, and, on EEG, slow activity with diffuse and nearly continuous spike activity. This condition often lasts for weeks and even months, with progressive worsening of cognitive functions, after which the patient is left with mental retardation and tonic seizures, mainly in early morning sleep, between 4:00 a.m. and 6:00 a.m.

*Id.* at 4.

Dr. Holmes noted that as a syndrome, “[Doose] does[ not] have a strict criteria [sic].” Tr. 296:2. When diagnosing someone after a seizure, Dr. Holmes explained that you have to first rule out a brain tumor and then “just wait and see because a lot of the children, — over 50 percent —, especially if you have a normal EEG will not, — which [D.J.W.] did — he — would not go on to have a second or a third seizure.” Tr. 306:19–22. Doose syndrome, “requires a number of features, including multiple seizure types,” and “a certain pattern on the EEG with spike and wave activity.” Tr. 307:10–13. In D.J.W.’s case, after the first seizure, there was eventually “a second seizure and perhaps that third seizure where [he was found] on the bathroom floor where he just sort of collapsed.” Tr. 306:25, 306:1. D.J.W. went on to have astatic seizures, “absence seizures where he stare[d] and blink[ed,] and then he ha[d] generalized tonic-clonic seizures.” Tr. 307:7–9. Dr. Holmes noted that “when all those things c[a]me together, [] I would have made the diagnosis of Doose syndrome, and I would have told [Petitioner] that I think this is most likely genetic.” Tr. 307:14–16.

Dr. Holmes explained that although not common, “cognition stagnation and delay [] can occur in Doose [patients] and especially [in] those children that have poorly controlled seizures.” Tr. 313:13–16. He distinguished seizures in conjunction with Doose syndrome from Dr. Shafrir’s discussion of autoimmune encephalitis. Tr. 248:18–249:8. Dr. Holmes clarified that encephalitis (brain inflammation), that is caused by autoantibodies (an immune system response), can lead to an encephalopathy (brain injury or dysfunction). Tr. 202:6–7, 13–14, 247:18–22. Dr. Holmes testified that Dr. Shafrir’s reference to encephalitis is not relevant to this case because there is no evidence that D.J.W. experienced brain inflammation. Tr. 266–68. Dr. Holmes noted on redirect

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<sup>26</sup> R. Nabbout & O. Dulac, *Epileptic Encephalopathies: A Brief Overview*, 20(6) J. CLIN. NEUROPHYSIOL. 393–97 (2003).

that in concluding that Doose syndrome accounted for all of D.J.W.'s symptoms, he was not including D.J.W.'s behavioral delays. Tr. 314:1–6.

Dr. Wiznitzer confirmed that D.J.W. has Doose syndrome in his written report and opined that the onset was following his first seizure reported on February 13, 2012. Resp't's Ex. E at 8. He reiterated Dr. Shafrir's contention that Doose syndrome has a genetic basis. *Id.* He noted that since 2010, "over [thirty] genes have been linked to Doose syndrome." *Id.* As a result, a recent proposal has emerged to "redesignate [Doose syndrome as a] genetic generalized epilepsy with MASs (myoclonic-atonic seizures), consistent with the familial genetic study conducted by Doose and the recent identification of candidate genes." *Id.*; Resp't's Ex. E7, ECF No. 124.<sup>27</sup>

### c. Autoimmune Encephalopathy

Dr. Shafrir opined in his first expert report that D.J.W. suffered from an autoimmune epileptic encephalopathy (Doose syndrome) that resulted from a vaccine-induced, immune response. Pet'r's Ex. 23 at 29. He discussed an article that "looked at the serum of autistic children" and identified antibodies to a protein that "is part of the neuronal potassium channel." *Id.*; Pet'r's Ex. 41, ECF No. 60.<sup>28</sup> Dr. Shafrir further explained that "[t]he only mechanism by which vaccines can cause neurological symptoms is through [the] activation of the immune system." Pet'r's Ex. 58 at 6.

Petitioner's causation theory hypothesizes that "[b]ecause of yet unidentified genetic susceptibility, D.J.W. reacted abnormally to his fifth DTaP vaccination by an immune attack on protein components of his brain, likely ion channels which control neuronal excitability[, and] produced progressive encephalopathy." Pet'r's Ex. 88 at 39. Dr. Shafrir explained that the encephalopathy manifested as seizures that continued to occur "because of the production of autoantibodies against brain components," via epitope spread and bystander activation. *Id.* In support of his theory, Dr. Shafrir identified the late onset of D.J.W.'s Doose syndrome as evidence that the temporal association between his vaccination and disease onset is not random. *Id.* Dr. Shafrir also noted that "inflammation has been implicated in the pathophysiology of childhood epileptic encephalopathies." *Id.* at 40. He identified the "increased production of inflammatory/epileptogenic cytokines in response to the DTaP vaccination" but noted that the "literature regarding [the] cytokine response to immunization is still not well developed." *Id.* Dr. Shafrir explained this is because "[t]he effects of autoantibodies on brain activity are much easier to study and characterize than the role of the cellular arm of the adaptive immune system and the innate immune system, [involving] multiple components, including multiple cytokines." *Id.* at 42. He continued that "[t]hese multiple components by themselves are covered by genetic and epigenetic mechanisms which are still poorly understood, and are regulated from mostly unknown interactions of cytokines, chemokines, and cell receptors." *Id.* Dr. Shafrir then noted that the DTaP vaccine "contained several proteins, as well as [an] aluminum adjuvant[,], which are capable of producing multiple cytokines, including those which were described in association with infantile spasms and probably other epileptic encephalopathies." *Id.*

<sup>27</sup> H. Oguni, *Epilepsy with myoclonic-atonic seizures, also known as Doose syndrome: Modification of the diagnostic criteria*, 36 EURO. J. PAEDIATRIC NEUROL. 37–50 (2022).

<sup>28</sup> D.F. Obregon, et al., *Potential Autoepitope with the Extracellular Region of Contactin-Associated Protein-like 2 in Mice*, 4(1) BRITISH J. MED. & MED. RES. 416–32 (2014).

In her pre-hearing submission, Petitioner described her causation theory as “well established in medical literature.” Pet’r’s Br. at 18. She continued:

There is evidence to suggest that the onset of the seizure is caused by an immunological mechanism. Through yet unidentified immunogenic traits, D.J.W. experienced an autoimmune injury in his brain, which was most probably mediated by either his innate and [sic] adaptive immune systems. The resultant autoimmune encephalopathy produced D.J.W.’s epileptic syndrome and residual neurological sequelae.

*Id.*

Dr. Shafrir testified that D.J.W.’s epileptic encephalopathy “more likely than not [has an] immune basis, and it is more likely than not that the vaccine was the trigger for the autoimmune process that caused it.” Tr. 76:1–3. When asked to describe the characteristics of autoimmune encephalopathy, Dr. Shafrir did not provide specific factors. He stated that “we see them based on the fact that there is [sic] some articles and it[ is] quite documented, and in many cases in which autoimmune basis was found[,] and Doose syndrome itself in one case report and in similar cases and in other case reports.” Tr. 76:15–18. When asked again for the evidence to support an autoimmune phenomenon in Doose syndrome, Dr. Shafrir explained, “most [kids with Doose syndrome] have problems before [onset], and – but it[ is] a generalized epilepsy that is associated with somewhat similar epileptic phenomena and is associated with worsening of cognitive function and are [sic] very severe.” Tr. 99:19–22. He later clarified, “there is no obvious relationship between epilepsies and autoimmune disease.” Tr. 100:22–23.

Dr. Shafrir testified that Doose syndrome is “not genetically based,” and “there are articles [that say] it is not.” Tr. 129:13–15; Pet’r’s Ex. 77, ECF No. 66.<sup>29</sup> Dr. Shafrir testified that articles support his contention that Doose syndrome has an autoimmune etiology. He asserted that the Sirsi et al. article sought to “widen the spectrum of etiologies for MAE to include autoimmunity.” Pet’r’s Ex. 77 at 1. The authors wrote that “a range of central and peripheral nervous system disorders” can result from autoimmunity to voltage gated potassium channel complexes<sup>30</sup> (“VGKC”). *Id.* at 4. “The proposed mechanism of pathogenicity is [the] binding of antibodies to transmembrane VGKCs which impair ion channel function leading to hyperexcitability.” *Id.* The authors described case studies but conceded that “the incidence, and the spectrum of VGKC autoimmunity in children is yet to be established.” *Id.* at 3. They further conceded that “there are no cases of VGKC antibody mediated epilepsy presenting as a MAE.” *Id.* at 4. One of the study’s stated limitations is that “multiple different intractable pediatric epilepsy syndromes [that] were not specific to MAE” were included. *Id.* The authors noted that “[a]lthough MAE is a unique[,] well-defined[,] electro-clinical syndrome, the underlying etiology is presumed to be genetic.” *Id.*

<sup>29</sup> D. Sirsi, et al., *Does Autoimmunity have a Role in Myoclonic Astatic Epilepsy? A Case Report of Voltage Gated Potassium Channel Mediated Seizures*, 1 ANN. CLIN. CASE REP. 1178–84 (2016).

<sup>30</sup> *Dorland’s* defines a voltage-gated channel as “an ion channel that opens or closes in response to changes in the electrical potential across the cell membrane.” *Dorland’s* at 337. The Sirsi et al. article is referring specifically to potassium channel complexes “of the peripheral nervous system [that] play an important role in synaptic transmission, conduction[,] and repolarization.” Pet’r’s Ex. 77 at 1.

Ultimately, they determined that “[c]ausality of MAE by VGKC antibodies needs further investigation and cautious interpretation.” *Id.*

Dr. Shafrir first described molecular mimicry as “the suggested mechanism” in this case in his written report. Pet’r’s Ex. 23 at 26. He asserted during his testimony that “molecular mimicry is definitely a solid place to start.” Tr. 107:16–17. Dr. Shafrir defined molecular mimicry as “a situation in which a part of the vaccine protein is similar to part of the target protein attacked by the autoimmune disease, and the antibody that is produced in the vaccine are [sic] attacking the protein that is similar in structure.” Tr. 106:14–18. He noted that bystander activation was another mechanism that he “mention[ed]” Tr. 106:24–25. He defined bystander activation as “an activation of other cells that are in the area of inflammation.” Tr. 106:25, 107:1. He continued with “the next [mechanism that] is something called an epitope spread [where] there is – because of inflammation that is caused by the immunoreaction, there is exposure of other parts of the molecule and the body – that they[ are] not supposed to be exposed, and then the body produce [sic] antibodies against them.” Tr. 107:2–6. Dr. Shafrir explained that he filed literature wherein the authors “look in databases of protein structure[s] and they look at [the] database of epitope[s] and of proven immune epitope[s] that were known to cause – to have antibodies against them, and they show that there is sharing of those structural vaccine[s] with those epitopes.” Tr. 107:19–23.<sup>31</sup> He conceded that none of the articles that he filed mentioned the DTaP vaccine or the corresponding wild viruses when discussing antibodies to the protein implicated in autoimmune epilepsy. Tr. 167:10–24.

When asked if there was any evidence of an autoimmune etiology in this case, Dr. Shafrir noted that a “treating physician actually suspected an autoimmune process existent, and it[ is] more or less [an] incomplete job.” Tr. 76:19–21. He opined that “the evaluation of autoimmune epilepsy was minimal, including only anti-NMDA receptor and anti-GAD (glutamic acid dehydrogenase) antibodies, measured only in the serum and not the [cerebrospinal fluid].” Pet’r’s Ex. 23 at 23. He continued, that “[i]mmunosuppressant treatment was initiated relatively early,” but noted that D.J.W.’s treatment “did not go beyond a single course of IVIG.” *Id.* Dr. Shafrir testified that no one looked for “any overt immune abnormality.” Tr. 117:10–11. Dr. Shafrir acknowledged that the medical records in this case did not contain “any generalized signs of autoimmunity.” Tr. 223:5–6. However, Dr. Shafrir asserted that in D.J.W.’s case, “he has Doose syndrome[,], and he ha[d] abrupt onset, very rapid cognitive decline, and — lack of response to medication typical to him.” Tr. 223:18–20. Dr. Shafrir also suggested that there was no attempt to determine if antibodies were present or there were any signs of encephalitis. Tr. 117:12–16. He stated that the minor child in this case “had nuances of progressive epileptic encephalopathies.” Tr. 125:2–3. According to Dr. Shafrir, this is “completely different, but it[ is] the same mechanism” as autoimmune encephalitis. Tr. 125:3–4.

Dr. Shafrir addressed the negative antibody testing in this case by discussing an article he submitted entitled, *Paediatric Autoimmune Encephalopathies: Clinical Features, Laboratory Investigations and Outcomes in Patients*, as evidence that the clinical presentation and response to treatment was similar in patients with or without antibodies. Tr. 85:23–25, 86:1; Pet’r’s Ex. 67,

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<sup>31</sup> Dr. Shafrir did not cite to any particular article when making this statement.

ECF No. 63.<sup>32</sup> Dr. Shafrir explained this observation applies to “the autoimmune encephalitis in those particular patients, but we have no reason to believe that it[ is] not — this does not exist in other situation [sic], and it is a work in progress.” Tr. 86:7–10. He highlighted that the three patients in the study had recently been vaccinated. However, Dr. Shafrir was reminded that all three of these patients also had “prodromal symptoms with either fever and/or associated infectious episodes.” Tr. 161:9–10. He admitted that D.J.W. did not have prodromal symptoms. Tr. 161:11–13. He further admitted that D.J.W. “does not fit the severe acute autoimmune encephalitis that [would lead] to [hospital] admission” seen in these types of cases. Tr. 163:6–7. However, Dr. Shafrir noted that D.J.W.’s “clinical presentation led his doctors to order tests for autoimmune encephalitis, so obviously his clinical presentation was compatible with this by the thinking of his neurologists as autoimmune encephalitis.” Tr. 163:12–15. Dr. Shafrir noted D.J.W.’s immunization “the week before” as the most important evidence of an autoimmune process in this case. Tr. 176:10. He also noted D.J.W.’s “abrupt onset of epileptic encephalopathy with uncontrolled seizure [sic] commingled with the other symptoms [a]s a reason to suspect autoimmune encephalitis.” Tr. 176:25, 177:1–4. He asserted that D.J.W. does “have autoimmune epilepsy. You can call it — so autoimmune encephalitis and autoimmune epilepsy can be both called autoimmune encephalopathy.” Tr. 136:8–10. Dr. Shafrir admitted that it is not generally accepted by the medical community that Doose syndrome is autoimmune. Tr. 137:16–18.

Following Dr. Shafrir’s direct and cross examinations, I asked him several questions to clarify his previous testimony. He defined encephalitis generally as, “signs of inflammation in the brain.” Tr. 201:5. I also asked for a definition<sup>33</sup> for encephalopathy. Dr. Shafrir defined encephalopathy as, “any abnormal function of the brain, more or less.” Tr. 202:3–4. When asked if his definition of the phrase ‘epileptic encephalopathy’ was consistent with the stand-alone definition of each word, Dr. Shafrir did not agree. Tr. 205:8–15. He described epileptic encephalopathy as an “independent term.” Tr. 204:15. He acknowledged that there is a formal, medical definition of the term but he “cannot [tell me what it is] by heart.” Tr. 206:1–3. He explained that “it has to do with that there is a contribute — the epileptic activity is producing some of the patient’s neurological deficit that would not exist if the epileptic activity would not exist.” Tr. 206:3–7. He described the deficit as consisting of “things that are not decisions but cognitive problem [sic] typically and regression in behavior, psychiatric problems.” Tr. 204:20–22.

Dr. Shafrir also clarified that Doose syndrome is not autoimmune encephalitis. Tr. 226:4. He maintained that Doose syndrome does have an autoimmune etiology, and that it manifests as an encephalopathy. Tr. 225:19–25, 226:1–4. After Petitioner’s testimony that D.J.W. suffered from a fever following vaccination, Dr. Shafrir asserted that the fever was of no consequence due to its common occurrence post vaccination. Tr. 232:10–12. Dr. Shafrir did not contend that evidence of D.J.W.’s fever strengthened Petitioner’s argument for an autoimmune etiology. *See* Tr. 232:17.

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<sup>32</sup> Y. Hacohen, et al., *Paediatric autoimmune encephalopathies: clinical features, laboratory investigations and outcomes in patients with or without antibodies to known central nervous system autoantigens*, 84 J. NEUROL. NEUROSURG. PSYCHIATRY 748–55 (2013).

<sup>33</sup> I also had Dr. Shafrir define epilepsy and autoimmune disease. He defined epilepsy as “having epileptic seizures[.]” Tr. 202:17–18. He defined autoimmune disease as a condition where a patient’s own immune system attacks a part of the patient’s body. Tr. 203:3–9.

Dr. Shafrir then admitted that the effect of making the DTP vaccine acellular was to “remove the factors that were determined to cause a lot of side effects,” including those commonly associated with autoimmune responses. Tr. 214:24–25. He went on to identify these side effects as a “[v]ery high fever, febrile seizure, encephalopathies, things like that.” Tr. 215:2–3.

Dr. Holmes disagreed that the etiology of D.J.W.’s epileptic encephalopathy is autoimmune. *See, e.g.*, Tr. 255:23–24. The Sirsi et al. article that Dr. Shafrir relied on specifically discussed patients with encephalopathy but who otherwise had “varying presentations including acute encephalitis, status epilepticus, febrile infection related epilepsy syndrome (“FIRES”)[,] and limbic encephalitis.” Pet’r’s Ex. 77 at 2. Dr. Holmes explained that Doose syndrome, by contrast, is an inherent encephalopathy and defined “inherent” as a “disorder in which the child is born with a predisposition to develop that syndrome.” Tr. 245:11–13. He noted that “head trauma can lead [to] epilepsy.” Tr. 277:4–5. However, he did not believe that D.J.W.’s fall off of the ladder played any part in his condition. Tr. 277:9. Dr. Holmes asserted that in the neurological community the “consensus is that [Doose syndrome has] a genetic cause.” Tr. 247:1. He explained “that there have been a number of genes identified in Doose syndrome, but the fact that it has a varying clinical presentation suggests that it[ is] probably multifactorial or polygenetic in cause, so there may be multiple genes that are coming together, unfortunately, in one child that leads to the epileptic encephalopathy.” Tr. 250:21–25, 251:1. Doose’s *Myoclonic-astatic epilepsy* chapter<sup>34</sup> supports Dr. Holmes’ contention. *See* Pet’r’s Ex. 63 at 4, ECF No. 63. Doose wrote, “[i]t has been demonstrated that a genetic predisposition to seizures of early childhood onset is the decisive factor in the pathogenesis of MAE.” *Id.* He continued, “[a] number of genetically distinct and partly mutually independent factors, some of which are expressed by special EEG patterns, others by certain clinical characteristics [,] are interacting and mutually augmentative.” *Id.* Dr. Holmes also cited Petitioner’s medical literature that reads, “MAE is an idiopathic[,], presumably genetic epileptic syndrome[,], with variable prognosis and although most [,] patients reach a seizure remission, the cognitive development remains uncertain.” *See* Pet’r’s Ex. 61 at 140, ECF No. 63.<sup>35</sup>

After Dr. Shafrir noted that physicians in this case considered an autoimmune etiology, Dr. Holmes countered that although D.J.W. received immunotherapy initially, D.J.W.’s current treatment plan does not involve steroids. Tr. 261:3–4. He stated he “[does] not believe [D.J.W.’s] current physicians believe he has an autoimmune epilepsy.” Tr. 261:17–19.

Dr. Holmes discussed the hypothesis that VGKC autoantibodies can lead to MAE and compared the child that had autoimmune seizure activity in the Sirsi et al. article to D.J.W. *See* Tr. 258–59; *see also* Pet’r’s Ex. 77.<sup>36</sup> Dr. Holmes testified that “there are certain children with Doose syndrome that can have an explosive onset of seizures, but it[ is] very unusual . . . for the child to come in basically with this many seizures, this refractory[,], and really not a good description of astatic seizures, which is part of the definition of Doose syndrome.” Tr. 259:18–23. The child in the Sirsi et al. case study had a generalized tonic-clonic seizure and was taken to the hospital. Tr.

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<sup>34</sup> MAE is Doose syndrome; however, the author had the grace to not use his own name in his work and in the chapter he authored. H. Doose, *Myoclonic-astatic epilepsy*, BENIGN LOCALIZED & GENERALIZED EPILEPSIES OF EARLY CHILDHOOD Ch. 25 at 166 (R. Degen & F.E. Dreifuss eds., 1992).

<sup>35</sup> M. Trivisano, et al., *Myoclonic astatic epilepsy: An age-dependent epileptic syndrome with favorable seizure outcome but variable cognitive evolution*, 97 EPILEPSY RES. 133–41 (2011).

<sup>36</sup> *See* D. Sirsi, et al., *supra* note 29.

258:9–10. In the hospital, the child “continued to have episodes [–] 5 to 45 seconds of staring, eye fluttering[,] and clonic movements.” Tr. 258:12–14. He experienced frequent seizures that were characterized by “bilateral upper extremity myoclonus, rapid eye fluttering, facial twitching[,] and subtle head drop.” Tr. 259:8–10. This child’s treaters believed he may have autoimmune encephalitis. Tr. 259:12–13. His antibody tests were negative, but “[h]e was treated with steroids and improved rapidly.” Tr. 259:15–16. Dr. Holmes testified that the case of the boy with autoimmune encephalitis “is quite different from [D.J.W.’s] case[.]” Tr. 259:17–18. He stated that there are so many differences between the case study and D.J.W. that while he “understand[s] why the authors [of the Sirsi et al. article] call this Doose syndrome, [he] would actually have some trouble with that.” Tr. 260:1–3.

Dr. Holmes continued to distinguish this case from the case studies submitted. *See, e.g.*, Pet’r’s Ex. 67 at 1;<sup>37</sup> Resp’t’s Ex. C, Tab 5, ECF No. 54.<sup>38</sup> Other patients with seizure disorders that have an autoimmune etiology “present with amnesia, confusion, seizures and psychiatric features, and some then develop a more generalized encephalopathy with a movement disorder.” *See* Resp’t’s Ex. C, Tab 5 at 1; *see also* Tr. 267:4–7. Dr. Holmes described what it might look like if there was evidence of autoantibodies in this case. He explained, “[i]t can look like a variety of manifestations, but usually the children have more than an isolated seizure.” Tr. 277:20–21. For example, Dr. Holmes testified that they “have changes in mental status, behavior, and encephalopathy . . . they may or may not have MRI changes, . . . they often have EEG abnormalities early on in the course.” Tr. 277:21–25.

Dr. Holmes testified that his opinion on D.J.W.’s condition is based on how he presented in the initial days and months following his first seizure. Tr. 268:4–8. Dr. Holmes clarified that his conclusions were not influenced by negative autoantibody testing. Tr. 268:2–8. Using the case studies relied on by Dr. Shafrir and the criteria for diagnosing Doose syndrome, Dr. Holmes concluded that D.J.W. suffered from severe Doose syndrome with seizures with no evidence of encephalitis or an autoimmune etiology. *See* Tr. 267–70.

Dr. Wiznitzer discussed the von Spiczak et al.<sup>39</sup> article that Dr. Shafrir relied on to support an association between vaccination and the development of Doose syndrome. *See* Resp’t’s Ex. E at 10; *see also* Pet’r’s Ex. 29 at 1, ECF No. 59. Dr. Wiznitzer noted in his post-hearing report that “the authors unequivocally state the overall risk for seizures, however, is not increased within [three] days following DTaP [vaccination],” and additionally, “the risk for epilepsies is not elevated even though epilepsy may present with a seizure following vaccination.” Resp’t’s Ex. E at 10; Pet’r’s Ex. 29 at 1.

Dr. Wiznitzer also discussed Dr. Shafrir’s reliance on the Kashiwagi et al.<sup>40</sup> article to explain the role cytokines may have played in a vaccine-induced, pathological, immune response

<sup>37</sup> *See* Y. Hachohen, et al., *supra* note 32, at 1.

<sup>38</sup> *See id.*

<sup>39</sup> S. von Spiczak, et al., *A retrospective population-based study on seizures related to childhood vaccination*, 52(8) *EPILEPSIA* 1506–12 (2011).

<sup>40</sup> Y. Kashiwagi, et al., *Production of inflammatory cytokines in response to diphtheria-pertussis-tetanus (DPT), haemophilus influenzae type b (Hib), and 7-valent pneumococcal (PCV7) vaccines*, 10(3) *HUMAN VACCINES & IMMUNOTHERAPEUTICS* 677–85 (2014).

in this case. Resp't's Ex. E at 11; Pet'r's Ex. 102, ECF No. 115. Cytokine levels, Dr. Wiznitzer asserted, peak approximately 24 hours post vaccination, and return to baseline within three days. Resp't's Ex. E at 11. D.J.W.'s first known seizure occurred seven days post vaccination, well after this three-day period. *Id.* Dr. Wiznitzer maintained the article, therefore, "does not show that any elevation [of cytokines] in humans would be high enough to cross the blood brain barrier and enter the brain," during that relevant post-vaccination, one-week time period in D.J.W.'s case. *Id.*

#### **d. Autism and Epilepsy**

Dr. Holmes explained that "[a] common biological mechanism for childhood epilepsy and comorbid ASD is suggested from their overlapping prevalence, which include subgroups of epilepsy and autism genes that have similar phenotypic manifestations and biological functions." Resp't's Ex. D at 2. Dr. Holmes noted the "known association of ASD with epilepsy for over fifty years, with the prevalence of epilepsy in ASD in some studies reaching almost 50%." *Id.*; Resp't's Ex. D2 at 1.<sup>41</sup> He cautioned that "[t]he high comorbidity rate between ASD and epilepsy and EEG epileptiform activity does not mean that there is a causal relationship between the conditions." Resp't's Ex. D at 2. Furthermore, "[s]eizure frequency is not associated with ASD, suggesting that treating seizures does not prevent ASD from emerging." *Id.*

Dr. Wiznitzer filed literature in support of the connection between ASD and epilepsy. He asserted that there is a known association between ASD and Doose syndrome and referred to the Routier et al.<sup>42</sup> and Tang et al.<sup>43</sup> articles for the premise that "the ASD diagnosis may be related to the developmental impact of the genetic causation beyond the effect of seizures and/or excessive epileptiform activity." Resp't's Ex. E at 9; Resp't's Exs. E3, E6, ECF No. 124. The Routier et al. article identified "four strong candidate genes [that] have already been linked to [ASD], [intellectual disability], and neurodegenerative brain disease." Resp't's Ex. E3 at 6. The authors concluded that "all patients with epilepsy genes or genes reported in neurodevelopment disorders showed [intellectual disability] and some presented later [with] ASD." *Id.* They determined that "this higher incidence of [intellectual disability] and ASD compared to the group with no identified genes might be related to the direct developmental impact of these genes beyond seizures and EEG impact." *Id.*

Dr. Wiznitzer concluded that ASD also has a genetic cause because of its relationship to Doose syndrome. Resp't's Ex. E at 9. The Tang et al. authors found that "[intellectual disability], ASD, and epilepsy share causative genes and biological pathways including gene transcription regulation, neurotransmission, and maintenance of synaptic structure." Resp't's Ex. E6 at 10. They continued that "[t]hese neurodevelopmental comorbidities may be a primary feature of the genetic disease rather than secondary to [the] disturbance of brain function due to excessive epileptiform activity (an epileptic encephalopathy)." *Id.*

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<sup>41</sup> A.W. Buckley & G.L. Holmes, *supra* note 24.

<sup>42</sup> L. Routier, et al., *Exome sequencing findings in 27 patients with myoclonic-atonic epilepsy: Is there a major genetic factor?* 96 CLIN. GEN. 254–60 (2019).

<sup>43</sup> S. Tang, et al., *Phenotypic and genetic spectrum of epilepsy with myoclonic atonic seizures*, 61 EPILEPSIA 995–1007 (2020).

## VI. Analysis

### A. D.J.W.'s Diagnoses

As a factual predicate to proving vaccine-causation, it is each petitioner's burden to demonstrate by a preponderant standard that the subject of the claim actually suffers from the injury alleged to have been caused by the identified vaccination(s). See *Hibbard v. Sec'y of Health & Hum. Servs.*, 698 F.3d 1358, 1364–65 (Fed. Cir. 2012); *Lombardi v. Sec'y of Health & Hum. Servs.*, 656 F.3d 1343, 1353 (Fed. Cir. 2011); *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1346 (Fed. Cir. 2010). D.J.W.'s diagnoses are in dispute not only between the parties in this case, but also between D.J.W.'s treaters and Petitioner's own expert. Although the various conditions asserted by medical professionals in this case may "present with many of the same symptoms, their underlying causes are different and require different treatments." See *Broekelschen*, 618 F.3d at 1344. To decide if Petitioner is entitled to damages, "it [i]s appropriate in this case—where virtually all of the evidence on causation [i]s dependent on the diagnosis of [D.J.W.'s] condition—for [me] to determine the proper diagnosis before applying the *Althen* test." *Id.*; *Althen v. Sec'y of the Dept. of Health & Hum. Servs.*, 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). Petitioner has alleged D.J.W. suffered from vaccine-caused epileptic encephalopathy and developmental delay. Furthermore, she connects the two injuries by asserting that there is a linear sequence of events from vaccination to seizures to delay.

There is no dispute that D.J.W. suffers from an epileptic encephalopathy. Petitioner alleges that this encephalopathy is the cause of D.J.W.'s developmental delay. D.J.W. has also been diagnosed with ASD. Petitioner's expert asserts that D.J.W.'s ASD was misdiagnosed, and all of his symptoms are explained by Doose syndrome. In her filings, Petitioner asserts that any autism diagnosis is unrelated to her claim and D.J.W.'s alleged vaccine-caused injuries. Respondent alleges that D.J.W.'s autism is the cause of the developmental delay. Respondent further asserts that Doose syndrome does not account for all of D.J.W.'s symptoms and as the two conditions are comorbidities, D.J.W. suffers from both ASD and Doose syndrome.

#### i. Autism Spectrum Disorder

D.J.W. was diagnosed with autism on May 22, 2019, by licensed clinical psychologist Dr. Carrie Silver. He was referred to Dr. Silver by his treating developmental behavioral pediatrician Dr. Nayfack. Dr. Silver opined that "[g]iven the full picture and review of available data, it is determined that [D.J.W.] does meet medical diagnostic criteria for an Autism Spectrum Disorder." Pet'r's Ex. 87 at 7. Furthermore, D.J.W.'s most recently filed medical records from a March of 2020 encounter with Dr. Nayfack note that "[t]esting confirmed moderate [intellectual disability] and autism." Pet'r's Ex. 109 at 27. An additional record from a November 9, 2021 evaluation with pediatric neurologist Dr. Jane MacLean lists epileptic encephalopathy, intellectual disability, and autism spectrum disorder in D.J.W.'s past medical history. Pet'r's Ex. 108 at 59. Dr. Shafrir presents robust arguments that D.J.W. does not suffer from autism, but from an autistic-like delay as a result of his epileptic encephalopathy. However, D.J.W.'s treaters have experience in diagnosing and treating autism. Furthermore, they have access to his medical and school records

and his family and medical histories. Lastly, their interactions with D.J.W. over a period of several years allow them to accurately diagnosis and treat his conditions.

The benefit of seeing a patient in person in addition to reviewing medical records cannot be overstated. Medical records created contemporaneously with the events they describe are generally trustworthy because they “contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions,” where “accuracy has an extra premium.” *Kirby v. Sec’y of Health & Hum. Servs.*, 997 F.3d 1378 (Fed. Cir. 2021) (citing *Cucuras v. Sec’y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993)). Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec’y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at \*20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). However, there is no presumption that medical records are accurate and complete as to all the patient’s physical conditions. *Kirby*, 997 F.3d at 1383 (citing *Cucuras*, 993 F.2d at 1528). Contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony — especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also* *Murphy v. Sec’y of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff’d per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. denied*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) (“[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.”)); *Althen*, 418 F.3d at 1278, 1280; *Andreu v. Sec’y of Health & Hum. Servs.*, 569 F.3d 1367, 1375–77 (Fed. Cir. 2009); *Capizzano v. Sec’y of Health & Hum. Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006) (“medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a ‘logical sequence of cause-and-effect show[s] that the vaccination was the reason for the injury.’”). However, medical records and/or statements of a treating physician’s views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. § 13(b)(1) (providing that “[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court”); *Snyder v. Sec’y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) (“there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct — that it must be accepted in its entirety and cannot be rebutted.”). Rather, special masters must consider the entire record. § 13(b)(1).

Dr. Silver’s examination and ultimate opinion concerning D.J.W.’s autism diagnosis is the result of behavioral evidence consistent with parental and treating physician suspicions. Despite D.J.W.’s simultaneous epileptic encephalopathy diagnosis, his current treaters separately recognize his autism diagnosis as reflected in his most current medical history. The experts in this case have presented evidence in support of their respective positions that is probative. However, Dr. Shafir’s position must be weighed against Dr. Silver’s first-hand diagnosis, Dr. Nayfack’s agreement, Drs. Holmes’ and Wiznitzer’s opinions, and the medical literature filed in this case. Considering the entire record, Petitioner has not established it more likely than not that D.J.W.’s autism was misdiagnosis. Therefore, I find preponderant evidence the D.J.W. suffers from autism.

## ii. Developmental Delay

To prevail on her claim that vaccinations caused D.J.W.'s developmental delay, Petitioner has to establish by a preponderance of the evidence that epileptic encephalopathy is the cause-in-fact, despite D.J.W.'s autism diagnosis. *See, e.g., Cedillo v. Sec'y of Health & Hum. Servs.*, No. 98-916V, 2009 WL 331968 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *aff'd*, 89 Fed. Cl. 158 (2009), *aff'd*, 617 F.3d 1328 (Fed. Cir. 2010); *Hazlehurst v. Sec'y of Health & Hum. Servs.*, No. 03-654V, 2009 WL 332306 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *aff'd*, 88 Fed. Cl. 473 (2009), *aff'd*, 604 F.3d 1343 (Fed. Cir. 2010); *Snyder v. Sec'y of Health & Hum. Servs.*, No. 01-162V, 2009 WL 332044 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *aff'd*, 88 Fed. Cl. 706 (2009); *Dwyer v. Sec'y of Health & Hum. Servs.*, No. 03-1202V, 2010 WL 892250 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); *King v. Sec'y of Health & Hum. Servs.*, No. 03-584V, 2010 WL 892296 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); *Mead v. Sec'y of Health & Hum. Servs.*, No. 03-215V, 2010 WL 892248 (Fed. Cl. Spec. Mstr. Mar. 12, 2010) (rejecting the contention raised in the Omnibus Autism Proceedings that vaccines can cause ASD); *see also Cunningham v. Sec'y of Health & Hum. Servs.*, No. 13-483V, 2017 WL 1174448, at \*4 (Fed. Cl. Spec. Mstr. Jan. 25, 2017) (rejecting Petitioner's attempt to separate a case alleging an autoimmune encephalopathy vaccine injury with other vaccine-autism cases because by doing so, it would create a step between vaccination and the end result of autism, simply to allow for compensation where other autism cases have failed); *Bushnell v. Sec'y of Health & Hum. Servs.*, No. 02-1648V, 2015 WL 4099824 (Fed. Cl. Spec. Mstr. June 12, 2015) (rejecting Petitioner's contention that neurotoxins contained in vaccines aggravated a minor child's mitochondrial disorder, resulting in a regressive encephalopathy manifesting as autism. The Court rejected the characterization of ASD as an encephalopathy or any other injury in an attempt to circumvent the binding effect of the Omnibus Autism Proceedings decision).

Although Petitioner now argues that the injuries alleged in the petition are solely related to epileptic encephalopathy, she acknowledges that D.J.W. has been diagnosed with autism. Pet'r's Mem. at 11. During his testimony, her own expert, Dr. Shafrir, conflated the clinical progression of D.J.W.'s autism with the increasing frequency and severity of his seizures. In fact, he was vehement that D.J.W. did not suffer from autism but displayed autistic symptoms as a direct result of the vaccine-induced seizures. Following D.J.W.'s diagnosis, Dr. Shafrir maintained his position and asserted that D.J.W. was misdiagnosed. In this case, Petitioner's expert's opinions provide some of the best evidence *against* her current argument.

Petitioner argues that she does not wish to recast her claim, but Dr. Shafrir's opinion that D.J.W. does not have autism is antithetical to D.J.W.'s current medical record. There is no way to reconcile Petitioner's current argument that D.J.W. suffers from "epileptic encephalopathy with developmental delay" and "also me[ets] the medical criteria for ASD[.]" Pet'r's Mem. at 11, with Petitioner's expert's opinion that "[a]utism is not an additional independent diagnosis in a patient who have [sic] already known severe progressive — regressive epileptic encephalopathy." Tr. 150:13–15. In fact, Petitioner's own tacit acknowledgement that D.J.W. does have autism contradicts Dr. Shafrir's final report where he reiterates that D.J.W. does not have autism. He asserts that D.J.W.'s "epileptic encephalopathy caused severe regression in all developmental aspects, including cognitive . . . [and] produced, among other things, the appearance of multiple autistic features." Pet'r's Ex. 88 at 45. Dr. Shafrir's assertion that epileptic encephalopathy cannot co-exist with autism contradicts much of the evidence, including, most notably, the filed literature.

Alternatively, the ASD diagnosis strengthens Dr. Holmes' argument that Doose syndrome does not explain D.J.W.'s behavioral and cognitive changes. Dr. Holmes opined that an individual could suffer from a severe case of Doose syndrome with accompanying seizures (epileptic encephalopathy) and a comorbid cognitive delay (autism). The Routier et al.<sup>44</sup> and Tang et al.<sup>45</sup> articles provide support for the premise that "the ASD diagnosis may be related to the developmental impact of the genetic causation beyond the effect of seizures and/or excessive epileptiform activity." Resp't's Ex. E at 9. The Routier et al. article concludes that "all patients with epilepsy genes or genes reported in neurodevelopment disorders showed [intellectual disability] and some presented later [with] ASD." See Resp't's Ex. E3.

Dr. Shafrir's testimony that D.J.W.'s autistic-like symptoms, which we now know to be autism, are a result of a vaccination, is also counter to a long line of Program cases that hold, without exception, that autism is not caused by vaccination. See *Cedillo*, 617 F.3d at 1328. Petitioner argues that other claims have been allowed to proceed on an alternative theory that encephalopathy caused intellectual disability following an autism diagnosis. Petitioner relies on a case where there is a developmental delay that clearly occurs within a different timeframe from the seizure activity. Pet'r's Mem. at 11; *Wright*, 2015 WL 6665600, at \*98. She cites a case wherein the claimant never alleges developmental delay as the injury caused by vaccination.<sup>46</sup> Pet'r's Mem. at 13–14; *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1324 (Fed. Cir. 2016). She also cites a case with clear evidence of encephalitis. Pet'r's Mem. at 16; *Mojabi v. Sec'y of Health & Hum. Servs.*, No. 06-227V, 2012 WL 6869685 (Fed. Cl. Spec. Mstr. Dec. 13, 2012). All of those cases are distinguishable from the facts here. The cases Petitioner relies on that were successful did not present evidence of autism symptoms that could not be parsed from those of encephalopathy. That is, however, precisely what Petitioner did in this case. In her reply to Respondent, Petitioner asserts "there is no dispute that D.J.W. developed epileptic encephalopathy, or unremitting epileptic activity that contributed to his severe and rapid cognitive and behavioral impairments, after his vaccination." Pet'r's Reply at 3. In the next paragraph, Petitioner asserts that "[t]he court is not required to find that D.J.W.'s subsequent diagnosis of autism was or was not caused by the vaccination." *Id.*

Petitioner has made it clear since sharing her initial concern of D.J.W.'s developmental delay with his physicians that the seizures and the regression occurred simultaneously. She has consistently argued that D.J.W.'s seizure activity and delay were both the result of his vaccination. Her current argument is that D.J.W.'s developmental delays resulted from seizures, which were unrelated to his autism diagnosis. She does not explicitly reject Dr. Shafrir's opinion that D.J.W. was misdiagnosed. It is unclear, however, whether Petitioner agrees with Dr. Shafrir that D.J.W. does not actually have ASD. She does not provide a legal argument to overcome the autism rulings that rejected the argument that developmental delay can be both a manifestation of an autism diagnosis and, independently, a result of vaccination. Indeed, this argument is not asserted in the successful cases she cites for support. See Pet'r's Mem. at 11–16. Further discussion of these cases highlight why they are distinguishable.

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<sup>44</sup> See L. Routier, et al., *supra* note 42.

<sup>45</sup> See S. Tang, et al., *supra* note 43.

<sup>46</sup> In the present case, Petitioner raised a possible significant aggravation claim in her petition, but that was never pursued. Petitioner's most recent post hearing filing alleges only causation-in-fact.

Petitioner cites to the *Wright* case as an example of a successful claim involving a child with autism who suffered from vaccine-caused encephalopathy. The child in that case suffered from a seizure within hours of vaccination and the encephalopathy fit within the criteria for a Table injury. *Wright*, 2015 WL 6665600, at \*98. In this case, the time lapse of seven days between D.J.W.'s vaccination and seizure precludes any claim based on a Table injury. *See, e.g., Adams ex rel. Adams v. Sec'y of Health & Hum. Servs.*, 76 Fed. Cl. 23, 41 (2007) (finding an infant who developed a febrile seizure within 24 hours of receiving a pneumococcal vaccination was entitled to compensation); *Tembenis ex rel. estate of Tembenis v. Sec'y of Health & Hum. Servs.*, No. 03-2820V, 2010 WL 5164324, at \*1, 2, 4, 15 (Fed. Cl. Spec. Mstr. Nov. 29, 2010) (finding a vaccinee who developed a fever and seizures within 12 hours of receiving a DTaP vaccination was entitled to compensation); *Teller v. Sec'y of Health & Hum. Servs.*, No. 06-804V, 2009 WL 255622, at \*2, 5 (Fed. Cl. Spec. Mstr. Jan. 13, 2009) (finding a vaccinee who developed a fever and seizures within 4 hours of receiving DTaP-IPV, Hepatitis B, pneumococcal, and Hib vaccinations was entitled to compensation); *Simon v. Sec'y of Health & Hum. Servs.*, No. 05-941V, 2007 WL 1772062, at \*2, 25 (Fed. Cl. Spec. Mstr. June 1, 2007) (finding a vaccinee who developed a fever and seizures within 12 hours of receiving a DTaP vaccination was entitled to compensation).

Petitioner also refers to *Moriarty* to argue that she can successfully bring a claim alleging an encephalopathy despite a comorbid autism diagnosis. *Moriarty v. Sec'y of Health & Hum. Servs.*, 130 Fed. Cl. 573 (2017). Petitioner discusses this case in some detail, but she fails to mention several significant distinguishing factors. Most importantly, in *Moriarty*, the child had already exhibited “problems with her gross motor skills and language development and was diagnosed with hypotonia and developmental delay” prior to the MMR vaccination at issue. *See Moriarty*, 844 F.3d at 1324. Petitioners in that case were able to cleanly differentiate between the developmental delay that their child had pre vaccination and the seizures that occurred post vaccination. This distinction was also evidenced by the successful treatment of the seizures with a ketogenic diet in that case, despite the continued developmental delay, i.e., autism. *Id.* at 1325. In the present case, D.J.W.'s seizures continued with “a grand mal seizure every week, and drop seizures up to 10–15 times a day as well as absence seizures daily,” despite a ketogenic diet. Pet. at 8. The continued seizures were accompanied by “issues with learning.” *Id.*

The nature of the seizures in *Moriarty* is also distinguishable from that in this case, and there is evidence that some treaters in *Moriarty* documented a belief that the MMR vaccination was to blame for the seizures. *Moriarty*, 130 Fed. Cl. at 576. All of these factors are evidence that the seizures in that case were not necessarily attributed to the child's autism. This is also evidenced by the petition itself. Petitioners in *Moriarty* alleged a seizure disorder and encephalopathy as the injury, but they did not include developmental delay. In the present case, Petitioner maintains that the autism diagnosis is separate from the encephalopathy, but she continues to assert that D.J.W.'s developmental delay is a vaccine-caused injury and not a result of his autism. *Moriarty* is not analogous to the present case and does not provide support for Petitioner's claim that D.J.W.'s autism diagnosis is separate from his encephalopathy.

The last case that Petitioner cites involves a child with encephalitis. *Mojabi*, 2012 WL 6869685, at \*1. There is no evidence in this case that D.J.W. was diagnosed with encephalitis, and Dr. Shafrir did not go as far as asserting that during his testimony. When asked what type of autoimmune encephalitis is present in this case, Dr. Shafrir responded that D.J.W. has

“autoimmune epilepsy. You can call it — so autoimmune encephalitis and autoimmune epilepsy can be both called autoimmune encephalopathy.” Tr. 136:8–10. He would not say that all three conditions could be used interchangeably and clarified that, “I think we can use more accurately autoimmune — auto — well, I mean, you can say that [he] have [sic] autoimmune epileptic encephalopathy. I think that[ is] the best way we can describe it.” Tr. 136:12–15.

Petitioner asserts that vaccinations caused or contributed to her child’s developmental delay, despite his autism diagnosis. Dr. Shafrir stated repeatedly that D.J.W.’s developmental delay was a result of encephalopathy, and he does not have autism. Respondent’s experts have explained, with supporting literature, that ASD and epileptic encephalopathy are comorbidities in the absence of vaccination. D.J.W.’s medical record is consistent with the explanations provided by Drs. Holmes and Wiznitzer. After considering the complete record, including Petitioner’s pleadings, medical records, expert reports and testimony, and medical literature,<sup>47</sup> I do not find preponderant evidence that D.J.W.’s developmental delay can be separated from his autism diagnosis. Therefore, I do not find that Petitioner has identified developmental delay as an actionable vaccine-caused injury in this case.

### iii. Epileptic Encephalopathy

Although Petitioner alleges a linear causation theory that links D.J.W.’s vaccine to his developmental delay via seizures, she also identifies epileptic encephalopathy as an actionable injury. Petitioner originally asserted that D.J.W.’s vaccination initiated an autoimmune response that resulted in seizures and ultimately epileptic encephalopathy, without regard for autism. Petitioner asserts and is correct that D.J.W.’s encephalopathy is not in dispute. There is disagreement, however, “on whether this can be caused by vaccination through an autoimmune process.” Pet’r’s Reply at 3. Therefore, Petitioner does have a viable claim based on epileptic encephalopathy, and my analysis will continue based on this injury. The entitlement hearing was conducted under the same premise.

## B. Applicable Legal Standards

Under the Vaccine Act, a petitioner may prevail in one of two ways. First, a petitioner may demonstrate that she suffered a “Table” injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the time period provided in the Table. § 11(c)(1)(C)(i). “In such a case, causation is presumed.” *Capizzano*, 440 F.3d at 1320 ; *see* § 13(a)(1)(B). Second, where the alleged

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<sup>47</sup> While I have reviewed all of the information filed in this case, only those filings, records, and testimony that are most relevant to the decision are discussed. *Moriarty v. Sec’y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) (“[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.”) (citation omitted); *see also Paterek v. Sec’y of Health & Hum. Servs.*, 527 F. App’x 875, 884 (Fed. Cir. 2013) (“[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.”).

injury is not listed in the Vaccine Injury Table, a petitioner may demonstrate that she suffered an “off-Table” injury. § 11(c)(1)(C)(ii). Petitioner does not assert a Table claim in this case.

In attempting to establish entitlement to a Vaccine Program award of compensation for an off-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*. *Althen* requires that a petitioner establish by preponderant evidence that the vaccinations she received caused her injury “by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.” 418 F.3d at 1278.

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a “reputable medical theory,” demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford v. Sec’y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006) (citations omitted). To satisfy this prong, a petitioner’s theory must be based on a “sound and reliable medical or scientific explanation.” *Knudsen v. Sec’y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be “legally probable, not medically or scientifically certain.” *Knudsen*, 35 F.3d at 549.

Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and, thus, scientific evidence offered to establish *Althen* prong one is viewed “not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act’s preponderant evidence standard.” *Andreu*, 569 F.3d at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec’y of Health & Hum. Servs.*, 121 Fed. Cl. 230, 245 (2015), *vacated on other grounds*, 844 F.3d 1363 (Fed. Cir. 2017). But this does not negate or reduce a petitioner’s ultimate burden to establish her overall entitlement to damages by preponderant evidence. *W.C. v. Sec’y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec’y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court’s opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. “In short, the requirement that an expert’s testimony pertain to ‘scientific knowledge’ establishes a standard of evidentiary reliability.” *Id.* at 590 (citation omitted). Thus, for Vaccine Act claims, a “special master is entitled to require some indicia of reliability to support the assertion of the expert witness.” *Moberly v. Sec’y of Health & Hum. Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010). The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec’y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) (emphasis in original) (“[U]niquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted.”).

Under *Daubert*, the factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has

been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community. *Terran ex rel. Terran v. Sec’y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 n.2 (Fed. Cir. 1999) (citing *Daubert*, 509 U.S. at 592–95). Nothing requires the acceptance of an expert’s conclusion “connected to existing data only by the *ipse dixit* of the expert,” especially if “there is simply too great an analytical gap between the data and the opinion proffered.” *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner’s medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77. The third *Althen* prong requires establishing a “proximate temporal relationship” between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase “medically-acceptable temporal relationship.” *Id.* A petitioner must offer “preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder’s etiology, it is medically acceptable to infer causation.” *de Bazan v. Sec’y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one’s requirement). *de Bazan*, 539 F.3d at 1352; *Shapiro v. Sec’y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff’d without op.*, 503 F. App’x 952 (Fed. Cir. 2013); *Koehn v. Sec’y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review denied* (Fed. Cl. 2013), *aff’d*, 773 F.3d 1239 (Fed. Cir. 2014). The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec’y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant v. Sec’y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992).

### **C. *Althen* Discussion**

#### **i. General Causation Theory (*Althen* prong one)**

Dr. Shafrir wrote that “[t]he only mechanism by which vaccines can cause neurological symptoms is through activation of the immune system.” Pet’r’s Ex. 58 at 6. Both experts testified that D.J.W.’s condition was an atypical presentation of Dose syndrome, but Dr. Shafrir did not present persuasive evidence of an autoimmune etiology. Dr. Shafrir’s discussion of encephalitis gave a very clear example of an autoimmune process, but he was unable to connect that mechanism with his theory in this case. Dr. Shafrir also confirmed that Dose syndrome is not autoimmune encephalitis. Given the severe and acute nature of autoimmune encephalitis, its treatment course, and clear markers for diagnosis, Dr. Shafrir did not persuasively explain why a discussion of autoimmune encephalitis is instructive in this case.

During his testimony Dr. Shafrir made a passing reference to several different mechanisms, including bystander activation and epitope spread, but stated that molecular mimicry “is definitely a solid place to start.” Tr. 107:16–17. To explain molecular mimicry, he embarked upon a meandering discussion about narcolepsy, adjuvants, and the whole cell pertussis vaccine. *See* Tr. 94–138. That testimony was tortuous and unhelpful to the facts and arguments in this case.

Therefore, it is not recounted in the summary of Dr. Shafrir's opinion. In short, the whole cell pertussis vaccine is no longer administered in the United States, and causation theories based on the enhanced immune response produced by adjuvants have been largely unsuccessful in the Program. *See, e.g., Decker v. Sec'y of Health & Hum. Servs.*, No. 15-017V, 2020 WL 7889059, at \*32 (Fed. Cl. Spec. Mstr. Dec. 14, 2020) (reiterating that “[aluminum adjuvant induced autoimmunity (“ASIA”)] is a theory that has been unsuccessfully argued [] in several previous [P]rogram cases.”). Lastly, while there is substantial evidence that narcolepsy may be an autoimmune disease, Dr. Shafrir, as with his encephalitis reference, did not present evidence that narcolepsy is analogous to Doose syndrome. I, and other special masters, have repeatedly warned petitioners that the mere mention of molecular mimicry is not a “get out of jail free card” in the Program, entitling claimants to compensation, merely because it has scientific reliability as a general matter. *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at \*26 (Fed. Cl. Spec. Mstr. Mar. 23, 2018) (“Petitioners cannot simply invoke the concept of molecular mimicry and call it a day . . . . Rather, they need to offer *reliable* and persuasive medical or scientific evidence of some kind . . . that suggests the vaccine components could interact with self-structures as maintained.”); *see also Haubner v. Sec'y of Health & Hum. Servs.*, No. 16-1426V, 2021 WL 5614942, at \*32 (Fed. Cl. Spec. Mstr. Oct. 22, 2021); *Sheets v. Sec'y of Health & Hum. Servs.*, No. 16-1173V, 2019 WL 2296212, at \*17 (Fed. Cl. Spec. Mstr. Apr. 30, 2019). This reasoning holds true for all biological mechanisms that are routinely presented in the Program.

Dr. Shafrir's explanations of bystander activation and epitope spread were also superficial and do not connect specifically to Doose syndrome. Petitioners are not required to identify specific biological mechanisms to establish causation. Indeed, scientific and “objective confirmation” of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; *see also Moberly*, 592 F.3d at 1322. However, as the Federal Circuit has made clear, “simply identifying a ‘plausible’ theory of causation is insufficient for a petitioner to meet her burden of proof.” *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Rather, “[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case.” *Moberly*, 592 F.3d at 1322.

Dr. Shafrir relied extensively and repeatedly on the Sirsi et al.<sup>48</sup> article to provide support for an autoimmune etiology for Doose syndrome. *See* Pet'r's Ex. 77. Dr. Holmes did not dispute that VGKC autoimmunity was a plausible pathogenesis for MAE; however, the Sirsi et al. article makes no mention of vaccination as a catalyst for the body's production of the relevant autoantibodies. Furthermore, those authors noted cases of multiple different intractable pediatric epilepsy syndromes, but there were no cases of VGKC antibody mediated epilepsy presenting as MAE. *See id.* The authors also conceded that unlike other pediatric epilepsies, the etiology for MAE is presumed to be genetic. *Id.* Dr. Shafrir, on the other hand, testified emphatically that Doose syndrome does not have a genetic etiology, but even the medical literature that he filed belies that assertion. *See id.*; *see also* Pet'r's Ex. 61.<sup>49</sup> Dr. Shafrir conceded during his testimony that the medical community has not generally accepted Doose syndrome as an autoimmune disease. Tr. 137:16–18. While the mechanism described in the Sirsi et al. article is currently a viable thought experiment, that is not the standard for establishing causation in Program cases. *See* Pet'r's Ex. 77. The authors themselves stopped short of identifying their proposed mechanism as causative and

<sup>48</sup> *See* D. Sirsi, et al., *supra* note 29.

<sup>49</sup> *See* M. Trivisano, et al., *supra* note 35.

suggested that further research is warranted. *See id.* Even assuming *arguendo* that the articulation of such a mechanism is sound and reliable, it is incomplete. Dr. Shafrir has not explained how vaccines fit into this immune process. His opinion that vaccines could be the catalyst for an untested, never-before-seen autoimmune etiology for a presumed genetic epileptic encephalopathy is speculative at best.

Petitioner's theory also includes a passing reference to increased cytokine production with a disclaimer that this type of mechanism is hard to study and understand. Dr. Shafrir asserted that "the persistence of the epileptic encephalopathy can be explained by several mechanisms including epitope spread and persistence of autoimmune activity with cellular or humoral autoimmune activity against adjacent proteins." *See Pet'r's Ex. 88 at 39.* This conclusion is an overbroad list of complex immune processes and concepts without relation to the specific characteristics of encephalopathy generally, or Dose syndrome specifically. Dr. Shafrir has not answered the question of how epitope spread is causal here. He did not explain how the different processes of cellular and humoral autoimmune activity interact during the pathogenesis of Dose syndrome post vaccination. There is no answer to the question, "can the DTaP vaccine cause Dose syndrome?" Evaluation of Petitioner's biological mechanism pursuant to the *Daubert* factors lays bare the theory's deficiencies. The theory, as best articulated in the Sirsi et al. article, has not been tested, and therefore, there is no known error rate or method to control error. Furthermore, the theory (VGKC autoimmunity in MAE) or even the premise (MAE has an autoimmune etiology) is not generally accepted by the relevant medical community.

Dr. Wiznitzer's discussion of the von Spiczak et al.<sup>50</sup> article, which illustrates that patients are not more likely to develop epilepsy post DTaP vaccination even if they experience a seizure shortly thereafter, is also persuasive evidence. *See Pet'r's Ex. 29.* Studies that establish or negate vaccine causation are extremely rare and not required in the Program. However, to the extent that studies have been done to analyze statistically significant cases of injury post vaccination, they are probative. It is worth noting that the von Spiczak et al. article is not significant in a vacuum. It is consistent with other submitted evidence that Dose syndrome is not an autoimmune disease and thus would be unlikely to result from vaccination via Petitioner's proposed mechanism. In sum, Petitioner has not presented preponderant evidence that a DTaP vaccination can cause Dose syndrome via his proposed biological mechanism. She has not met her burden pursuant to *Althen* prong one.

## **ii. Logical Sequence of Cause and Effect (*Althen* prong two)**

Dr. Shafrir's asserted biological mechanism begins with the premise that D.J.W. experienced an abnormal reaction to his fifth DTaP vaccination, resulting in "an immune attack on protein components of his brain." *Pet'r's Ex. 88 at 39.* The applicability of Petitioner's causation theory to the present case therefore hinges on an autoimmune etiology for D.J.W.'s Dose syndrome. D.J.W.'s current treatment is not indicative of an autoimmune disease. Dr. Shafrir even acknowledged that there was no evidence in D.J.W.'s medical record of general autoimmunity. *Tr. 223:5-6.* I am not persuaded by Dr. Shafrir's heavy reliance on D.J.W.'s treaters' initial consideration of an autoimmune process, given the ultimate diagnosis and treatment regimen. D.J.W. underwent cursory testing for an autoimmune etiology that did not yield definitive results.

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<sup>50</sup> *See S. von Spiczak, et al., supra* note 39.

D.J.W.'s treatment course of a single round of IVIG for autoimmune seizure activity was ineffective and discontinued. Dr. Shafrir noted that Petitioner refused further IVIG treatment, but the record does not reflect a concern from D.J.W.'s treaters that this directive significantly hindered D.J.W.'s treatment. While it is reasonable, given D.J.W.'s presentation, that medical providers would initially administer IVIG, the cessation of this treatment without concern from treaters is significant. Furthermore, as stated previously, Petitioner has not presented preponderant evidence that Doose syndrome can ever result from vaccination.

Alternatively, Dr. Holmes opined that D.J.W.'s specific epileptic encephalopathy, Doose syndrome, is an inherent condition. He further explained that there is no evidence of an autoimmune etiology in this case and described what he would look for to diagnose a patient with autoimmune seizure activity. Dr. Holmes identified several symptoms, including amnesia, confusion, seizures and psychiatric features, a more generalized encephalopathy with a movement disorder, MRI changes, and early EEG abnormalities. None of these additional factors were present in D.J.W.'s case. Dr. Holmes' use of case studies and other medical literature for support also increases the credibility of his opinion. In particular, the literature that explains how the medical community has come to believe that Doose syndrome has a genetic etiology, is persuasive. *See, e.g., Resp't's Ex. E7.*<sup>51</sup> Dr. Holmes presented persuasive medical literature from Doose himself to support his testimony that Doose syndrome is a multifactorial, genetic condition. *See Pet'r's Ex. 63.* Therefore, Petitioner has failed to establish by preponderant evidence that D.J.W.'s epileptic encephalopathy has an autoimmune etiology. This, by Dr. Shafrir's explicit admission, is a necessary condition for Petitioner's suggested biological mechanism of injury. Therefore, I find Petitioner has failed to establish by a preponderant standard that the vaccine causation theory presented is relevant to the injury suffered by D.J.W. Petitioner has not met her burden pursuant to *Althen* prong two.

### iii. Timing (*Althen* prong three)

Petitioner has failed to meet her burden with respect to *Althen* prong one. This makes it difficult to determine an appropriate temporal relationship between vaccination and the alleged injury pursuant to prong three. In this case, however, Dr. Shafrir stated that the seven-day period between D.J.W.'s DTaP vaccination and his first seizure is compelling. Respondent's experts noted the same short interval as temporally proximate. However, as it has been settled in the Program, a temporal relationship alone is not sufficient to establish causation. However, I find that Petitioner's assertion that a seven-day-interval would be sufficient time for an adaptive immune response to develop post-vaccination to be appropriate. I find that Petitioner has therefore satisfied her burden with respect to *Althen* prong three, to the extent that an autoimmune process could develop within that time.

## VII. Conclusion

Petitioner and her son have both been through immeasurable suffering and uncertainty since this case was filed. The delay in clarifying his diagnosis, as well as other logistical and administrative delays, have undoubtedly added to the stress. In the Program, the multifactorial pathogenesis of many of the diseases that we see is frustrating and can be difficult for us to

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<sup>51</sup> *See* H. Oguni, *supra* note 27.

understand. That is why the expert opinions and supporting medical literature are so important in helping me reach a decision. After a careful consideration of all the filed evidence in the record (medical records, expert reports, and medical literature), along with the presented testimony, I find that Petitioner has had an opportunity to present the case that D.J.W. developed a vaccine-caused, autoimmune encephalopathy. This evidence was not submitted in contemplation of an autism diagnosis (as Petitioner requested), and Petitioner had the opportunity to present her complete argument at a hearing. This opportunity is further evinced by the fact that Petitioner's expert did not change his position at any point, including after the hearing, D.J.W.'s autism diagnosis, and Respondent's post-hearing expert opinions. Special masters possess discretion to decide whether an evidentiary hearing will be held. 42 U.S.C. § 300aa-12(d)(3)(B)(v) (promulgated as Vaccine Rule 8(c) & (d)); *Kreizenbeck v. Sec'y of Health & Hum. Servs.*, 945 F.3d 1362, 1365 (Fed. Cir. 2018). Given Petitioner's opportunity to present expert evidence pre hearing, at hearing, and post hearing, I do not find an additional hearing is needed, largely due to Dr. Shafrir's assertion that D.J.W.'s autism was misdiagnosed and is therefore inconsequential. Based on the record in this case, Petitioner has failed to present preponderant evidence that D.J.W.'s autism exists independently from his epileptic encephalopathy, or that his encephalopathy has an autoimmune pathogenesis and can therefore be vaccine-caused. I do not find that additional evidence would be able to overcome the evidence already in the record on those two points. Accordingly, Petitioner has failed to establish entitlement to compensation and her claim is hereby **DISMISSED**. The Clerk of Court shall enter judgment accordingly.<sup>52</sup>

**IT IS SO ORDERED.**

s/Herbrina D. Sanders  
Herbrina D. Sanders  
Special Master

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<sup>52</sup> Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.